JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXVI SEPTEMBER, 1937 No. 9

HENRY G. RUENZEL.

The Honorary President of the AMERICAN PHARMACEUTICAL ASSOCIATION was born July 18, 1861, in Milwaukee, Wis., the son of Mr. and Mrs. Frederick Ruenzel (*née* Bartels). His early education was obtained in the parochial school of Trinity Church in Milwaukee. At the age of 14, he entered the employ of Gustavus Bode, a refiner of gold and silver and analytical chemist, with whom he remained for two years, learning how to assay, analyze and do general analytical work.

At the age of sixteen years he engaged with the firm of Widule and Conrath as an apprentice in Pharmacy and he has continued as retail pharmacist in the profession up to the present time.

In the fall of 1883, Mr. Ruenzel entered the University of Wisconsin by examination as member of the first pharmacy class, graduating in 1885, and honored as the medalist of this class. In 1925 the University of Wisconsin conferred on him the honorary degree of "Master of Pharmacy."

Mr. Ruenzel joined the Wisconsin Pharmaceutical Association in 1892. The subjects of his contributions were largely on home-grown drugs, including digitalis and stramonium; during the experimental age, he raised 100 per cent stramonium over a period of four years, as per assay at the University of Wisconsin.

In 1892, Mr. Ruenzel joined the AMERICAN PHARMACEUTICAL ASSOCIATION and became a *Life Member*, March 28, 1928, and served as delegate to its annual meetings.

In 1902, he was appointed member of the State Board of Pharmacy by Governor Robert M. LaFollete, Senior, and remained an active member until April 19, 1937; for twenty-five years he was secretary of the Wisconsin Board and has represented the Board since the National Association of Boards of Pharmacy was founded. At the Montreal meeting he was elected first honorary president of the National Association.

On August 23, 1887, the subject of this sketch married Sophia von Meyer, of Milwaukee; they celebrated their Golden Wedding Anniversary on August 23, 1937. Four children—Louise, Carl, Fred and Margaret—have added happiness to the home.

EDITORIAL

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PROGRESS OF PHARMACY.

THE SHAPING of all professions is dependent largely on how well the foundations are laid and on the relative number who take an earnest part in the promotion. The development and the changes follow the direction given by the leaders and the influences brought about by enactments.

These facts can be compared with the ideas that are put into practice in government; differing decidedly from those that were factors and have been displaced by other control. These have their influence in nearly all, if not all activities. In general, many fundamental thoughts remain, but there are changes that bring about professional or business conduct which shape the course.

President S. R. Atkins of the British Pharmaceutical Conference fifty years ago gave a forecast relative to British pharmaceutical practice and the following quotation is from the *Chemist and Druggist* of September 4, 1937.

> "We may see again in Great Britain the days of commercial, industrial and agricultural prosperity we so long enjoyed, but we shall never return to the easy-going times of the past. We have entered on a new, if not a better, order of things; the competition of the age must be reckoned with as a permanent factor; let us hope that the survival of the fittest will be the result. The future condition of pharmacy in this country (Great Britain) in all probability will be developed on the scientific and semi-professional side. Pharmacists are trained to the manipulation of a large number of minute transactions involving much care and no small anxiety, but each one financially of small moment. Such operations have no tendency to develop the business man in the ordinary acceptation of the term. The conditions of the average pharmacy are opposed to the habit of broad generalization, so essential to success in other callings. I am not despondent as to the future, but I feel that our hope lies in cultivating the scientific rather than the merely trading side of pharmacy, for in this direction, from the nature of things, competition will be less acute, and remuneration for service rendered on a higher scale."

Quoting the last two paragraphs of the Introduction of the report of Chairman Ray Lyman Wilbur for the Committee on the Costs of Medical Care:

"*The quality of medical care is an index of a civilization.*[1] When in earlier centuries the entire time and energy of a people were consumed in providing food, clothing and shelter there was little left for the care of the sick and disabled. As the margin between production and the needs of mere subsistence expanded, the preservation of health was one of the first needs to receive attention. To-day in American civilization, health occupies a high place among accepted social values. As we emerge from the present depression and build up a surplus of income not necessary for mere subsistence, we shall do well to realize that we can invest this surplus is no better way than in the preservation of health.

"*Our physical and mental health is perhaps the nation's greatest asset.* It behooves each community, therefore, to consider what plan will most effectively promote the health of its citizens. To each and every community in the United States

[1] Italics ours.

which desires to provide better medical care and increased health for all its people, the Committee offers these recommendations. The report affords for the first time a scientific basis on which the people of every locality can attack the perplexing problem of providing adequate medical care for all persons at costs within their means. It is hoped that the report may thus aid materially in bringing greater health, efficiency and happiness to all the people."

Resolutions of the AMERICAN PHARMACEUTICAL ASSOCIATION were published in the August JOURNAL, page 772; Nos. 4, 5 and 7 deal with plans for the coördination of pharmaceutical interests; distribution of medicaments through retail pharmacists; approval of efforts by U. S. Public Health Service. These actions and the parts from President Atkins' address and other quotations have a bearing on the activities of pharmacy and may mark its practice.

Quoting James H. Beal:[1] "Is it not possible that we have devoted too little attention to the adjustment of pharmacists to the rapidly changing condition of modern civilization?"

The continued progress of pharmacy is dependent on the measure of its professional practice—the adaptation of new ways and modern methods of service.

The problems of pharmacy, as of other activities, must be solved more by research and less by tradition. The recent health program shows that the growth in both demand and frequency of human coöperation has increased in proportion to the progress of civilization, and as a participant in the undertaking pharmacy should not be weakened in its possibilities but strengthened, so that it may continue in its service. For that purpose the AMERICAN PHARMACEUTICAL ASSOCIATION adopted the resolution bearing on the subject.

The schools of pharmacy and the bodies concerned with supervision of its practice are looking ahead with plans for higher education and training with the thought uppermost that those who engage in the practice must be qualified for solving the future problems of pharmacy, realizing that pharmacy is in close relation with other professions engaged in public health service and those in contributory sciences.

What the future of pharmacy will be, depends to no small extent upon an understanding of its history and a thoughtful program which directs to progress. The problems of the future will, no doubt, be as important as those of the past and, probably, present as many difficulties.

PHARMACY IN CHINA.

Professor E. N. Meuser, head of the Pharmacy School of West China Union, was a registrant at the meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION and a visitor at the AMERICAN INSTITUTE OF PHARMACY.

The venture is well worth while and Professor Meuser is hopeful that he may receive contributions from the United States, Canada and England for a pharmacy building that will encourage the proposition and will enable the faculty and university to improve their teaching facilities. There are opportunities in commerce which would be strengthened by such coöperation.

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[1] March JOURNAL, A. PH. A., page 279.

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins; H. M. Burlage, W. G. Crockett, E. V. Lynn, C. O. Lee, L. W. Rising, L. W. Rowe, Heber W. Youngken, F. V. Lofgren, J. C. Krantz, Jr. (To Be Revised.)

A COMPARATIVE STUDY OF THE PHARMACOLOGICAL ACTIONS OF NATURAL AND SYNTHETIC CAMPHOR.*,[1]

BY B. V. CHRISTENSEN[2] AND HAROLD J. LYNCH.[3]

INTRODUCTION.

During the past several years camphor has acquired an especial interest because of the wide divergence of opinion concerning its pharmacological behavior and clinical efficiency and more recently because of the growing tendency to replace natural products by synthetically prepared materials which are identical in physical and chemical properties. The replacement of natural Japanese camphor by synthetic camphor has occurred quite extensively in the industries and the synthetic form has been included in the eleventh revision of the United States Pharmacopœia.

Some observers are of the opinion, based on experimental evidence, that no difference whatever exists between natural camphor and synthetic camphor in their pharmacologic actions and on this basis can see no reason why synthetic camphor cannot replace natural camphor in therapeutics. On the other hand, others claim that synthetic camphor is more toxic than the natural product and should not be used unless absolutely necessary and then only cautiously.

The published clinical reports on synthetic camphor are few and the details somewhat meager. Some clinicians feel that it is fully as effective as natural camphor in cardiac and circulatory diseases and the replacement of natural camphor by the synthetic product fully justifiable. On the other hand, other investigators feel that on the basis of the experimental results which show that the synthetic camphor is more toxic than natural camphor and the absence of adequate clinical reports, the substitution of synthetic camphor for natural camphor in therapeutics seems unwarranted where no absolute necessity exists or at any rate until further observations are made and the discrepancies in the evidence cleared up. These experimental and clinical contradictions and disagreements prompted the undertaking of this study.

DIFFERENCES OF OPINION CONCERNING THE PHARMACOLOGICAL ACTIONS.

The earliest investigators on this subject, Langaard and Maass (1), using preparations of dextro, lævo and racemic camphor were able to obtain an excitation of the central nervous system in frogs with all three forms. They found that in this respect the lævo was the most powerful, the dextro the least, and the racemic intermediate between the two.

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* Scientific Section, A. PH. A., Dallas meeting, 1936.

[1] From a dissertation presented to the Graduate Council of the University of Florida, July 1935, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[2] Director, School of Pharmacy, and Professor of Pharmacognosy & Pharmacology, University of Florida, Gainesville, Florida.

[3] Graduate assistant in Pharmacognosy & Pharmacology, University of Florida, 1931–1935.

Pari (2) showed lævo camphor to be thirteen times more toxic than the dextro form and concluded that inasmuch as synthetic camphor is composed of a mixture of both dextro and lævo camphor the racemic compound would be more toxic than the natural dextro camphor. This point particularly emphasized the necessity of careful research before the synthetic camphor can be considered therapeutically equivalent to the natural dextro camphor.

Sargin (3) maintains that all three isomers of camphor have a similar action. However, he found the fatal dose of lævo camphor to be 20 per cent smaller than that of dextro camphor.

Joachimoglu (4), one of the foremost workers in this field, compared the three stereoisomers of camphor and concluded that no difference exists between them in regard to toxicity and that the synthetic camphor is tolerated by the organism just as well as is the dextro form.

Joachimoglu (5) in further work using smooth muscle of the leech found that the three isomers produced qualitatively and quantitatively the same effect.

Ramirez (6) concluded that the pharmacodynamic similarity of natural and synthetic camphor as regards their effects on the blood pressure, renal output, respiration, vessels and hearts of frogs and dogs is so great that no differences may be established between them using the current methods of investigation. On the basis of his experimentation Ramirez claims that this similarity would justify the use of either one of the camphors in clinical work.

EXPERIMENTAL.

Relative Toxicities of Synthetic and Natural Camphor.—In order to determine the relative toxicities of synthetic and natural camphor a series of experiments were performed using white rats.

The minimum lethal dose of synthetic camphor for white rats was found to be smaller than that of natural camphor; namely, synthetic camphor 1.7 mg./Gm. (Table I), and natural camphor 2.2 mg./Gm. (Table II). The accompanying tables include the experiments just above and below the found minimum lethal doses. In order to facilitate the tabulation of the results it was found convenient to note the time after the injection required for the appearance of the first symptom such as jerking and trembling, the time after the injection for the first convulsion to occur and also the time required to produce death.

TABLE I.—MINIMUM LETHAL DOSE OF SYNTHETIC CAMPHOR FOR WHITE RATS. THE CAMPHOR, IN A 20 PER CENT SOLUTION IN OLIVE OIL, INJECTED UNDER THE SKIN OF THE BACK OR FLANK. "R"—RECOVERY. "D"—DEATH.

Rat No.	Wt. in Grams.	Milligrams per Gram Injected.	Milligrams Injected.	First Symptom, Minutes.	First Convulsion, Minutes.	Death or Recovery in Hours.
5	156	1.5	234	13	68	R
7	156	1.6	251	17	33	R
*10	132	1.7	224	20	24	D-27.5
17	178	1.8	320	21	31	D-25.0
21	262	2.0	524	21	50	D-19.5

* M. L. D.

TABLE II.—MINIMUM LETHAL DOSE OF NATURAL CAMPHOR FOR WHITE RATS. THE CAMPHOR, IN A 20 PER CENT SOLUTION IN OLIVE OIL, INJECTED UNDER THE SKIN OF THE BACK OR FLANK. "R"—RECOVERY. "D"—DEATH.

Rat No.	Wt. in Grams.	Milligrams per Gram Injected.	Milligrams Injected.	First Symptom, Minutes.	First Convulsion, Minutes.	Death or Recovery in Hours.
1	112	2.1	235	6	32	R
* 7	180	2.2	396	42	55	D-42
13	260	2.3	598	24	35	D-30
19	229	2.4	549	17	40	D-31.5
21	157	2.6	408	9	34	D-28

* M. L. D.

These experiments also indicated that the action of synthetic and natural camphor is primarily upon the central nervous system and that there is no qualitative difference in their action. However, quantitatively there is considerable difference in that the minimum lethal dose of synthetic camphor is 1.7 mg. per Gm. of body weight of rat while that of natural camphor is 2.2 mg. per Gm. of body weight of rat. Further, the action of synthetic camphor develops more rapidly and causes death sooner than does natural camphor. Death with both kinds of camphor is due to respiratory failure.

Action of Synthetic Camphor on the Normal Frog Heart.—A 1–1000 solution of synthetic camphor in 0.6 per cent salt solution and frogs weighing from 20 to 30 Gm. were used. In order to eliminate the temperature factor the frogs and all solutions used were kept at room temperature. One cc. of the 1–1000 solution was dropped on the exposed frog heart at intervals of 15 minutes and short tracings taken at intervals of 3 minutes.

Synthetic camphor has a marked effect on the rate and amplitude of the frog heart. (Fig. 1 and 2.)

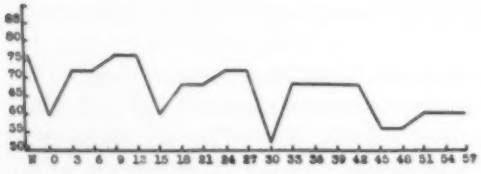

Fig. 1.—Rate curve of typical effect of synthetic camphor, 1–1000 solution, on the normal frog heart (Exp. 1). Ordinate: Beats per minute; Abscissa: Time in minutes; N: Normal. Synthetic camphor applied at N, 12, 27 and 42.

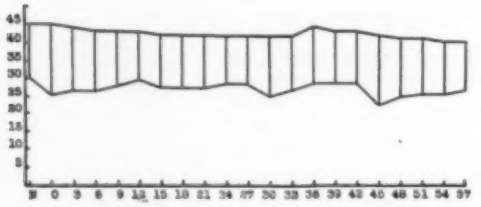

Fig. 2.—Amplitude curve of typical effect of synthetic camphor, 1–1000 solution, on the normal frog heart (Exp. 1). Ordinate: Amplitude in mm. (x 4); Abscissa: Time in minutes; N: Normal. The vertical lines represent the height of a tracing made with a lever attached to the ventricle of the frog heart and also its relation to the base line. Synthetic camphor applied at N, 12, 27 and 42.

Fig. 3.—Rate curve showing typical effect of perfusing the isolated rabbit heart with a 1–5000 solution of synthetic camphor (Exp. 54). Ordinate: Beats per minute; Abscissa: Time in minutes; N: Normal. Synthetic camphor solution perfused at N; replaced with Ringer's solution at 1.

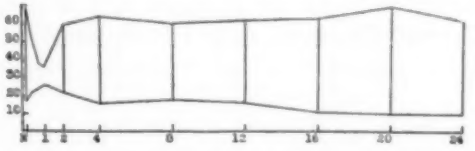

Fig. 4.—Amplitude curve showing the typical effect of perfusing the isolated rabbit heart with a 1–5000 solution of synthetic camphor (Exp. 54). Ordinate: Amplitude in mm.; Abscissa: Time in minutes; N: Normal. Synthetic camphor solution perfused at N; replaced with Ringer's solution at 1.

The heart rate was found to decrease and then increase but not back to the normal level. As the experiments proceeded and more synthetic camphor was ad-

ministered the rate decrease from the high level of the preceding period became less, but still dropped more and more below the normal. Decrease in rate varied from 4 to 28 beats per minute. The amplitude of the excursion of the frog heart showed an increase to above normal, either staying there or falling back to the normal level after a short time. The increases in the amplitude were usually in the diastolic direction. It was noted that the slowing of the beat of the normal frog heart by synthetic camphor was compensated for by the increase in the amplitude, thus producing a slower but stronger beat. The progression toward the diastolic line indicates a loss of muscle tone.

Action of Natural Camphor on the Normal Frog Heart.—The same procedure was followed as in the preceding but with a 1–1000 solution of natural camphor.

It was found that natural camphor had some effect on the rate and amplitude although it was not as pronounced as that produced by synthetic camphor.

Following the first application of natural camphor to the frog heart the rate decreased. Decrease in rate varied between 4 and 24 beats per minute. The decrease in rate was followed by an increase but the normal rate was never regained. Second, third and fourth applications produced essentially the same effect as the first, the rate decreasing in every instance from that of the preceding.

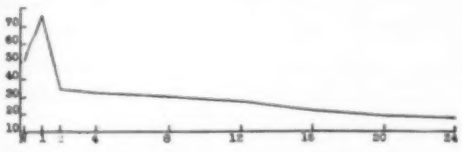

Fig. 5.—Curve showing the typical effect on the coronary flow of perfusing the isolated rabbit heart with a 1–5000 solution of synthetic camphor (Exp. 54). Ordinate: Cc. per minute; Abscissa: Time in minutes; N: Normal. Synthetic camphor solution perfused at N; replaced with Ringer's solution at 1.

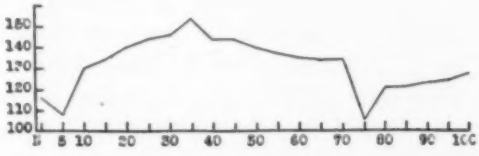

Fig. 6.—Blood pressure curve showing the typical effect of intravenous injections of synthetic camphor on the cat (Exp. 73). Injections: 5 mg./Kg. at N; 10 mg./Kg. at 35; 20 mg./Kg. at 70. Ordinate: Blood pressure in mm. of Hg; Abscissa: Time in minutes; N: Normal.

The first application of natural camphor caused an increase in the amplitude of the excursion of the frog heart and in all cases the increase was toward the diastolic lines.

A second, third and fourth application produced essentially the same effect as the first application, the amplitude increasing in every instance from the preceding period. This increase varied from 1 to 3.5 mm. and was toward the diastolic line in every case.

From the data herein presented it will be seen that although the action of the two camphors is essentially the same qualitatively, the synthetic camphor has a more powerful action on the normal frog heart in slowing the beat and increasing the amplitude of the excursion than has natural camphor.

Action on the Isolated Perfused Rabbit Heart.—For perfusing the isolated rabbit heart the method and apparatus of Gunn (7) was used.

Varying concentrations of synthetic camphor in Ringer's solution were used, *i. e.*, 1–1000, 1–5000 and 1–10,000, several experiments being carried out with each concentration. After a

normal tracing was obtained the synthetic camphor solution was turned on and allowed to remain on until the point of maximum effect was reached when the Ringer's solution was again turned on, replacing the synthetic camphor solution.

Perfusion of the isolated rabbit heart with varying concentrations of *synthetic* camphor produced an immediate increase in *rate*. Upon changing to Ringer's solution this increase in rate was followed in every instance by a fall back to or below normal and this in turn was followed by an increase back to or slightly above the normal rate. The greatest changes in rate were produced by the strongest solution (1–1000) and the least by the weakest solution (1–10,000). (Fig. 3.)

With respect to the *amplitude*, all concentrations of synthetic camphor used produced a distinct fall. The fall was the greatest with the 1–1000 solution and the least with the 1–10,000 solutions. The initial fall was followed by an increase to above normal when the synthetic camphor solution was replaced by Ringer's solution. This increase was maintained at or above the normal until the end of the experiment. (Fig. 4.)

With all concentrations used the initial change in amplitude was in the diastolic direction. Replacement of the synthetic camphor solution with Ringer's solution produced an increase in the systolic direction.

All concentrations of synthetic camphor used produced an increase in the coronary output in all the experiments performed, the extent of increase being in the direction of the greatest concentration. Replacement of the synthetic camphor solution with Ringer's solution produced in all cases a decrease in the rate of flow back to or below the normal. (Fig. 5.)

The initial fall in amplitude is compensated for by the initial increase in the rate and the fall in rate is in turn compensated for by the increase in amplitude. The amplitude change in the diastolic direction indicates a loss of muscle tone while the recovery in the systolic direction suggests a stronger and more complete contraction, indicating perhaps an increase in the tonicity of the cardiac muscle.

From the above it will be seen that after an initial, pronounced depressant effect, synthetic camphor stimulates slightly the heart of the rabbit, the action presumably being on the heart muscle. The coronary vessels exhibit a dilation due to the effect of the synthetic camphor. This dilation is then followed by a constriction, as evidenced by the decreased coronary output.

The same procedure was followed using natural camphor. All concentrations of *natural* camphor when perfused through the isolated rabbit heart produced an immediate increase in *rate*. The greatest changes in rate were produced by the strongest concentrations.

The *amplitude* of the rabbit heart with all concentrations used suffered a marked fall in all cases and again the strongest solution produced the greatest effect. The direction of the amplitude change was in the diastolic direction. Replacement of the natural camphor solution with Ringer's solution brought about recovery in the systolic direction.

Perfusion with all concentrations produced an increase in the *coronary* output, the greatest increase occurring with the strongest solution. This increase indicates a dilation of the coronary vessels. Increase was followed by a gradual decrease to below the normal, due perhaps to a constriction of the coronary vessels.

The initial fall in amplitude is compensated for by the increase in rate and

the fall in rate by the increase in amplitude. That the coronary vessels are dilated is indicated by the increased flow. This, however, is followed by a constriction, thus producing the diminished flow which was observed.

From the above it will be seen that the action of synthetic and natural camphor on the perfused isolated mammalian heart is essentially qualitatively alike. However, that synthetic camphor has a more powerful action is evident from the more pronounced changes in rate, amplitude, coronary flow and the shorter time required to produce these changes. With synthetic camphor the heart appeared to have an improved tonicity in that at the end of every experiment the heart was in a state of greater contraction than the normal, whereas, with natural camphor only a few were in a state of greater contraction at the conclusion of the experiment than when normal and then only slightly so.

Action on the Mammalian Circulation and Respiration.—Cats anesthetized with urethane, 0.9 Gm./Kg. orally about a half-hour before the operation, were used in these experiments. During the operation it was found advisable to give a little ether.

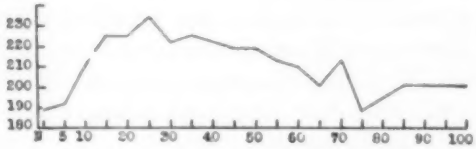

Fig. 7.—Heart rate curve showing the typical effect of intravenous injections of synthetic camphor on the cat (Exp. 73). Injections: 5 mg./Kg. at N; 10 mg./Kg. at 35; 20 mg./Kg. at 70. Ordinate: Heart rate per minute; Abscissa: Time in minutes; N: Normal.

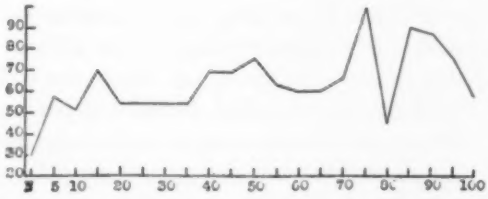

Fig. 8.—Respiratory rate curve showing the typical effect of intravenous injections of synthetic camphor on the cat (Exp. 73). Injections: 5 mg./Kg. at N; 10 mg./Kg. at 35; 20 mg./Kg. at 70. Ordinate: Rate per minute; Abscissa: Time in minutes; N: Normal.

For the intravenous injections the femoral vein was exposed and a cannula, attached by means of a short rubber tube to a burette containing Normal Salt Solution, tied in. Injections were made through the walls of the rubber tube and the solution washed into the vein by letting in a little salt solution. All injections were kept below 2 cc. in volume.

Intravenously, doses of 5, 10 and 20 mg. of *synthetic* camphor in a 1 or 2 per cent solution in olive oil per Kg. of cat were administered, thus taking care not to give a convulsive dose. The dose of 5 mg./Kg. was calculated to be about equivalent to the usual subcutaneous dose in man.

Following the intravenous injection of 5 mg./Kg. the blood pressure, after a slight preliminary fall, rose to above the normal where it remained until the end of the 30-minute period. (Fig. 6.) The preliminary fall occurred in from 1 to 3 minutes and ranged between 2 and 8 mm. of Hg. After 2 to 10 minutes the blood pressure returned to normal and above, and 30 minutes after the injection was between 8 and 30 mm. of Hg. above the normal level. The intravenous injection of 10 mg./Kg. produced a similar although more pronounced effect. (Fig. 6.)

The injection of 20 mg./Kg. produced in all instances a marked fall in blood pressure of from 31 to 100 mm. in from 1 to 3 minutes. This was then followed in all cases by a rise but the blood pressure after 30 minutes, remained considerably below the original normal. (Fig. 6.)

Following intravenous injection of 5 mg./Kg., the heart rate, after a slight preliminary fall of from 3 to 6 beats per minute, increased gradually and at the end of the half-hour period was from 21 to 33 beats per minute above the normal. (Fig. 7.)

The injection of 10 mg./Kg. intravenously produced in about half of the experiments a preliminary fall followed by a still greater rise than was noted after the first injection. In the other experiments the rate after a slight increase fell steadily.

The intravenous injection of 20 mg./Kg. produced in the majority of the experiments an immediate and marked fall in heart rate to considerably below the original normal. This was then followed by an increase up to or slightly below the normal. (Fig. 7.)

The intravenous injection of 5 mg./Kg. caused an immediate increase in the *respiratory* rate. This was then followed by a decrease but at the end of the period the respiration was still above the normal. (Fig. 8.) The maximum rate was reached in about 2 or 3 minutes and ranged between 12 and 39 inhalations (or exhalations) per minute. The depth of the respiration was also increased.

The injection of 10 mg./Kg. produced very much the same effect except that it was more pronounced and more prolonged.

With 20 mg./Kg. a still greater and more prolonged effect was produced than with the former injections. In all the experiments the respiratory rate increased immediately, reaching the maximum in from 1 to 2 minutes, the rate increase ranging between 39 and 93 inhalations per minute. (Fig. 8.) The depth of the respiration again showed an appreciable increase over the former injections.

The *blood pressure* of the cat following the intravenous injection of synthetic camphor behaved according to the dose administered. Small doses, 5 mg./Kg., which approximates the usual human subcutaneous dose, produced, after a slight preliminary fall, a considerable increase in the blood pressure. Larger doses, 10 mg./Kg., as a rule produced a fall in blood pressure although the blood pressure still remained above the normal. With still larger doses, 30 mg./Kg., the blood pressure suffered a marked fall, the subsequent rise not regaining the normal level.

After subcutaneous injections of synthetic camphor, 0.2 Gm./Kg., a gradual increase in blood pressure was observed. This was followed by a gradual fall to below the normal level in from 30 to 50 minutes where it remained until the end of the two-hour period. Absorption was apparently complete in from 30 minutes to 1 hour. The effect came on slower but was more prolonged than with the intravenous injections.

The increase in blood pressure following the intravenous injection of 5 mg./Kg. may possibly be accounted for by the increased heart rate, the increased rate being due to a direct stimulation of the heart muscle since it has been shown in previous experiments that perfusion of the isolated mammalian heart with varying concentrations of synthetic camphor produced an increase in heart rate. The fall in blood pressure following the administration of a larger dose, 10 mg./Kg., despite the fact that the heart rate still increased, is probably due to a direct systemic vasodilator effect. It will be remembered that the coronary blood vessels of the isolated mammalian heart were dilated after perfusion with solutions of synthetic camphor. The still greater fall in blood pressure after the intravenous injection of 20 mg./Kg. might be attributed to a more pronounced vasodilator effect and also to the marked slowing of the heart which was evident. This slowing may be due to a direct depres-

sant effect on the heart muscle since the concentration of synthetic camphor in the system had reached a rather high level after the last injection.

Similarly the increase in blood pressure following the subcutaneous injection of synthetic camphor, 0.2 Gm./Kg., might be attributed to the increased heart rate. The fall which occurred can likewise be attributed, despite the increased heart rate, to a systemic vasodilator action in that absorption was usually complete in from one-half to one hour and about this time the blood pressure began to fall and continued to do so until, after two hours, it was considerably below the normal level.

The most pronounced and consistent effect of synthetic camphor was noted on the respiration. The intravenous injection of all doses, 5, 10 and 20 mg./Kg., produced in every instance an immediate and marked increase in the depth and rate of respiration. The largest dose, 20 mg./Kg., produced the most pronounced and lasting effect and conversely, the smallest dose, 5 mg./Kg., the least effect. However, in almost every instance, regardless of the dose administered, the respiratory rate at the conclusion of the experiment was still above the normal.

With subcutaneous injections of synthetic camphor, 0.2 Gm./Kg., the same effects on the respiration were noted as in the case of the intravenous injections except that they were not as pronounced nor did they come on as quickly. However, the effect was more prolonged.

The same procedure was followed as in the preceding, using *natural* camphor solutions. It was observed that natural camphor produced qualitatively similar effects but that synthetic camphor is more potent quantitatively.

The comparative effects of synthetic and natural camphor upon the mammalian circulation and respiration may be summarized as follows:

A.—After small intravenous doses, synthetic camphor produces a marked stimulation of the circulatory system as shown by the increased blood pressure due possibly to an increased heart rate which may be due to a direct action on the heart muscle and despite any vasodilation. Natural camphor, on the other hand, after small intravenous doses, produces a more or less depressant effect on the circulation as shown by the fall in blood pressure due perhaps to a systemic vasodilation and despite the increased heart rate.

B.—Larger intravenous doses of both synthetic and natural camphor produce a marked depression of the mammalian circulation as evidenced by the marked lowering of the blood pressure and decrease in heart rate. The effect of synthetic camphor is more prompt, more pronounced and more lasting than that of natural camphor.

C.—Synthetic camphor, subcutaneously, after a more or less brief stimulant effect on the circulation as shown by the increased blood pressure, due possibly to an increased heart rate despite any vasodilation, has a depressant effect on the mammalian circulation as shown by the decrease in blood pressure due possibly to an increased vasodilation and despite the increased heart rate. Natural camphor, on the other hand, after subcutaneous injections has a marked depressant effect as shown by the fall in blood pressure due possibly to a systematic vasodilation and despite the increased heart rate. The effects of synthetic camphor here also are more pronounced than those of natural camphor.

D.—Both synthetic and natural camphor, intravenously and subcutaneously, have a marked stimulant effect on the mammalian respiration as shown by the increased rate and depth. However, the effects of synthetic camphor are more pronounced and more lasting than those of natural camphor.

SUMMARY AND CONCLUSIONS.

1. The minimum lethal dose of synthetic camphor for white rats is 1.7 mg. per Gm. while that of the official natural camphor is 2.2 mg. per Gm. of body weight

of rat. Both synthetic and natural camphor act chiefly on the central nervous system, death being due to respiratory paralysis.

2. Both synthetic and natural camphor cause a depressant action on the normal frog heart.

3. Neither synthetic camphor nor natural camphor is of value in overcoming the effect of chloral hydrate on the frog heart.

4. Both synthetic camphor and natural camphor primarily depress the perfused isolated mammalian heart.

5. The effect of intravenous and subcutaneous injections of both synthetic and natural camphor on the circulation is chiefly depressant.

6. Both synthetic and natural camphor markedly stimulate the mammalian respiration.

7. The differences in action between synthetic camphor and natural camphor are chiefly quantitative and not qualitative, synthetic camphor having a more pronounced and powerful action.

8. It appears logical and justifiable from the experimental evidence obtained to substitute synthetic camphor for natural camphor for medicinal purposes.

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THE ANTHRONE DERIVED FROM BARBALOIN AND ISOBARBALOIN.*

BY JOHN H. GARDNER[1] AND LIONEL JOSEPH.

More than twenty years ago, Léger (1) presented evidence that the common varieties of aloin are mixtures of two isomers, barbaloin and isobarbaloin. The aloin sold in this country is prepared from Curaçao aloe and is made up largely of barbaloin with a smaller but still considerable proportion of isobarbaloin.

These isomers resemble each other closely in most of their properties. They have the same percentage composition, melting point and crystal form. The most notable differences are, *first*, isobarbaloin is much more soluble in methyl alcohol than is barbaloin, and *second*, isobarbaloin gives a Klunge reaction (a red color with aqueous sodium chloride and copper sulfate) in a few minutes whereas with barbaloin the color appears only after a half hour or longer. Léger also describes a number of cases in which the corresponding derivatives of the two substances dif-

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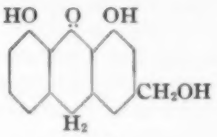
[1] This investigation was made possible by a grant to the senior author from a fund given to Washington University by the Rockefeller Foundation for research in science.

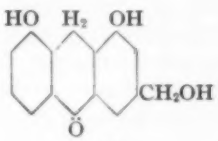
fer, but for the most part these derivatives do not have satisfactory properties for the establishment with certainty of their purity or uniformity.

Several years ago, Hauser (2) showed that barbaloin yields an aloe-emodin anthrone on hydrolysis with an aqueous solution of borax. Later, this compound was shown by Rosenthaler (3) and by McDonnell and Gardner (4) to be aloe-emodin-9-anthrone,[1] (Formula I). Hauser in his original article suggested that



I

barbaloin and isobarbaloin might be derived from the two isomeric aloe-emodin-anthrones. If this view were correct, isobarbaloin should yield aloe-emodin-10-anthrone (Formula II) on hydrolysis.



II

In order to check this hypothesis, commercial aloin was fractionally crystallized from methyl alchol, giving four fractions. The two least soluble were combined and freed of isobarbaloin by Léger's method (1) involving subjection to the Klunge reaction. Samples of all fractions were then hydrolyzed with aqueous borax solution. The products so obtained were purified and then reduced with stannous chloride, tin and hydrochloric acid to the corresponding chrysophanic acid anthrone, and finally acetylated. The final product in all cases proved to be chrysophanic acid-9-anthranol triacetate, identical with the compound synthesized by Naylor and Gardner. This demonstrates conclusively that both barbaloin and isobarbaloin yield aloe-emodin-9-anthrone (Formula I) on hydrolysis with aqueous borax, showing that the structural difference between the two must be accounted for on some other basis than a difference in the anthracene nucleus.

EXPERIMENTAL.

Separation of Barbaloin and Isobarbaloin.—Fifty grams of commercial aloin were dissolved in 400 cc. of hot methyl alcohol. Upon cooling, yellow crystals separated (Fraction I). After filtering out Fraction I, the mother liquor was concentrated to 200 cc. Fraction II crystallized out

[1] In a paper published about a year ago, Léger (5) criticized one of us for calling this compound aloe-emodin-9-anthrone rather than aloe-emodin-9-anthranol. It should be pointed out that Meyer and Sander (6) have shown that in the tautomeric mixture of 1-hydroxy-9-anthrone and 1-hydroxy-9-anthranol, there is a scarcely detectable amount of the anthranol, despite the fact that all of the reactions expected of 1-hydroxy-9-anthranol are given. By analogy, it seems probable that the product derived from barbaloin exists chiefly in the anthrone form. Consequently, we will continue to call it aloe-emodin-9-anthrone, recognizing, however, that it is probably a mixture of that substance with a small quantity of the corresponding anthranol in dynamic equilibrium.

on cooling and was separated by filtration. The mother liquor was again concentrated to 100 cc. and Fraction III which separated on cooling was separated. Further concentration to about 25 cc. gave a mass which solidified on cooling (Fraction IV). All concentrations were carried out in a partial vacuum without access of air.

Fractions I and II were combined and dissolved in 500 cc. of hot water to which had been added 75 Gm. of sodium chloride and 25 cc. of a saturated solution of copper sulfate. The solution was heated on a boiling water-bath for ten minutes. A red color developed very quickly. Upon cooling, long yellow needles separated and were filtered from the red solution. This process was repeated until the mother liquors were no longer colored red. The dried needles were recrystallized from a mixture of two volumes of chloroform and one volume of methyl alcohol. The product corresponded in all details with Léger's description of barbaloin.

Fractions III and IV were recrystallized from methyl alcohol. Fraction IV was fairly pure isobarbaloin and Fraction III almost certainly a mixture of the two compounds.

Hydrolysis.—Each of the three fractions (Barbaloin, Fraction III and Fraction IV) was hydrolyzed with aqueous borax following Hauser's procedure (2). After thirty minutes of boiling, the solutions were acidified with hydrochloric acid and the precipitates dried and extracted with boiling toluene. The yellow crystals which separated on cooling the toluene extracts were recrystallized from 75 per cent acetic acid. All products melted within the range 198° to 201.5°. Aloe-emodin-9-anthrone melts at 201–202.5° (McDonnell and Gardner (4)).

Reduction of the Hydrolysis Products.—The specimens of aloe-emodin-9-anthrone so obtained were reduced to the corresponding chrysophanic acid anthrone with stannous chloride, tin and hydrochloric acid in glacial acetic acid solution following the procedure of McDonnell and Gardner (4). The products were recrystallized from glacial acetic acid.

Acetylation.—Each of the three specimens of chrysophanic acid-9-anthrone derived ultimately from the three aloin fractions was acetylated in the usual way with acetic anhydride and sodium acetate and the acetates were recrystallized from glacial acetic acid. Melting points alone and mixed with equal amounts of chrysophanic acid-9-anthranol triacetate (m. p. 239.8–241°) were determined. All melting points agreed within reasonable experimental and there was no depression in any case, indicating that all products were identical with chrysophanic acid-9-anthranol triacetate and with each other. All melting points were corrected. The values are given in Table I.

TABLE I.

MELTING POINTS OF THE PRODUCTS FROM THE ALOIN FRACTIONS ALONE AND WITH CHRYSOPHANIC ACID-9-ANTHRANOL TRIACETATE.

Fraction.	M. P. Alone.	M. P. Mixed.
Barbaloin	240.8–241.2	239.8–240.2
III	240.8–241.5	239.6–240.4
IV	239.4–239.8	239.6–241.0

SUMMARY.

It has been shown that all fractions obtained by the fractional crystallization of commercial aloin yield aloe-emodin-9-anthrone on hydrolysis with aqueous borax solution demonstrating that barbaloin and isobarbaloin are not derivatives of isomeric anthrones.

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THE EFFECTS OF INDIVIDUAL ENVIRONMENTAL FACTORS ON THE CHEMICAL CONSTITUENTS OF PLANTS.

I. GLUCOSIDE OF FLAX.*,[1]

BY NOEL M. FERGUSON.[2]

INTRODUCTION.

For many years the interest of a considerable number of plant physiologists has been centered on the rôle played by certain climatic factors upon the chemical constituents of plants.

Among the earlier workers might be mentioned Collins and Blair (1) whose experiments tended to prove that certainly temperature and perhaps moisture as well were effective in varying the chemical constitution of flax. They found that seeds of flax plants which were grown in hot, dry climates yielded a higher quantity of HCN than seeds obtained from plants growing in temperate regions. Then followed a number of investigations dealing with glucosidal and alkaloidal plants other than flax. Among the more recent were two researches which have a direct bearing on the effect of ultraviolet light upon the glucosides in *Digitalis purpurea L.*

The first of these is the work of Miss McCrea (2) which deals with the effects of ultraviolet light upon the glucosidal content of *Digitalis purpurea L.*, in which it is claimed that plants grown under Vitaglass for a given length of time and then placed in the field produced more physiologically active constituents than those grown under window glass and then placed in the field.

The second research on *Digitalis purpurea L.*, carried out by Arthur and Leonard (3) which tends to disprove that of Miss McCrea, does not appear to have been successful since the comparisons are unconvincing. Due to the fact that the two experiments were carried out under somewhat different conditions and in both investigations there were uncontrolled factors, a comparison is impossible.

With these facts in mind the writer became interested in knowing just what effect the climatic conditions, moisture and light, and artificial light of certain wavelengths have in changing the glucosidal content of flax.

EXPERIMENTAL.

The flax was sown in flats and allowed to germinate under ordinary greenhouse conditions. For each series of sets thirty flats were prepared of which the twenty-five healthiest were used. Five of these served for the low moisture experiment and will be designated hereafter as Set "A," five for high moisture, designated as Set "B," five for the control condition, designated as Set "C," five for the low light, designated as Set "D" and five flats for the high light, designated as Set "E."

In all there were four series of sets, the last of which was used for the raying experiment. These series of sets were prepared sixteen days apart so as to have them growing over a long period of time, thus ruling out any variations which might exist in temperature and length of day. The

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* Scientific Section, A. PH. A., Dallas meeting, 1936.

[1] Abstracted from a thesis representing work done in the Shaw School of Botany submitted to the Board of Graduate Studies of Washington University by Noel M. Ferguson in partial fulfilment of the requirements for the degree of Master of Science.

[2] Assistant Professor of Botany and Pharmacognosy, St. Louis College of Pharmacy.

plants were all grown under the same conditions of temperature and humidity. The average temperature was about 65° C.

Sets "A," "B" and "C" were placed in an east room in the greenhouse which was not an end room. Therefore, any light which came in from the north, south or west had to pass through two thicknesses of glass. The sets were rotated within this room so that all of them received an equal supply of light. Sets "D" and "E" were placed in the end room adjoining the room containing Sets "A," "B" and "C" and consequently received more light since one side faces east and the end south. Here also the flats in each set were rotated in order to insure the plants an equal supply of light.

Assays were run on each series of sets for three consecutive weeks, beginning two weeks after germination, *i. e.*, one week after the experiment was started.

The amount of moisture added to Set "A" and Set "B" was varied from that added to the control set by paying particular attention to the condition of the plants in these sets. Set "B" was much greener than Set "A," and showed less tendency to wilt. The percentage of moisture in the soil of these three sets was also determined and the amount of water was added in such quantities as to give Set "A" a very small amount of soil moisture, Set "B" a great amount of soil moisture and the control set, Set "C," an amount midway between that found in Sets "A" and "B."

That the method of watering produced different water contents of the plants is shown by the following table of dry-weight percentages of the three sets.

TABLE I.

Series.	Set "A."	Set "B."	Set "C."
I	21.0 %	13.47%	15.96%
II	13.4 %	9.7 %	11.8 %
III	13.96%	10.8 %	11.65%
III_2	13.07%	8.3 %	9.6 %

In Sets "D" and "E" the light conditions were varied, thereby also changing the rate of transpiration and consequently the percentage of soil moisture.

During the germination period and up to the time the experiment was started, all of the plants received the same amount of light and moisture. The temperature conditions were also the same. In order to reduce the variations to a minimum the plants were rotated about the room and particular attention was paid to the brightness of the day in order that each plant might receive the same amount of light.

At the beginning of the experiment the flats known as Set "D," were placed under cheesecloth curtains which, according to photometric measurements, reduced the amount of light to approximately one-half. Set "E" was placed in the same room and received full light.

The only variable which might then exist between Sets "D" and "E" besides that of light, is humidity and its effects on the soil moisture. The latter was adjusted, however, by means of atmometer readings (4). The variation in temperature was so slight that no provision was made for its control other than that of growing the sets over a long period of time.

As a source of additional irradiation the G. E. Sun Ray Lamp (S-I), (5) with a high transmission of visible and ultraviolet radiations in the regions of 3000 to 4000 Å was used. These irradiations when applied during the daytime were supplementary to daylight. It was equipped with a tray filter consisting of Red Purple Ultra glass No. 597 of 5 mm. thickness containing a 2-cm. layer of distilled water, fitted closely to the reflector of the lamp. This allows for a slight transmission of ultraviolet from about 3130 Å to a slight transmission of the violet line at 4050 Å with a high transmission, about 85%, at 3650 Å. There is also a slight amount of extreme red at 7500 Å, transmitted by the glass. Thus essentially only the long ultraviolet radiations reached the plants from the lamp.

The accompanying Fig. 1 indicates the percentage of transmission of the various wavelengths of light by this glass (6).

The raying distance was standardized at 23 cm. from the tops of the plants to the bottom of the filter.

The plants to be assayed were cut off just below the cotyledons. Only average plants were taken for assay. Ten grams were quickly weighed off very accurately in a weighing bottle which

was then placed in the drying oven at a temperature of 118° C. and dried for twenty-four hours. Upon reweighing the percentage of dry-weight was calculated. The remainder of the green material was immediately weighed, ground in a cold room to prevent the liberation of HCN and placed in the generator. The amount of green material assayed was the same for all sets. On the basis of the dry-weight percentage of each lot of material to be assayed, the actual dry-weight was calculated and this weight was used in arriving at the percentage of glucoside present.

The plants were ground and the grinder washed with 150 cc. of distilled water. This material, to which had been added two drops of caprylic alcohol to prevent frothing, was then placed in the generator which consisted of a 1000-cc. sidearm, Erlenmeyer flask, fitted with a gas-tight, motor-driven stirrer, having a $^1/_{32}$" bore to allow for aeration (7). A delivery tube leading from the sidearm conducted the gas into a train of three absorption bottles equipped with Folin's ammonia tubes and containing a 5% KOH solution (8). A stream of air was sucked through the whole apparatus, while the stirrer was turning, thus conducting the HCN, liberated by the action of the enzyme, linase (9) on the glucoside, into the absorption bottles where it formed a weak KCN solution. Aeration was continued for eighteen to twenty-five hours. Shortly before the end of the assay 15 cc. of 20 per cent HNO_3 was added to each generator to insure the elimination of all of the HCN. Aeration was resumed for $^1/_2$ hour after the addition of the acid.

The absorption bottles were emptied and rinsed into a 500-cc. wide-mouth Florence flask. To the flask was then added 10 drops of a 5% KI solution and the KCN titrated with one-hundredth normal silver nitrate solution in a manner similar to that reported by Bishop (10). This consisted in adding the silver nitrate solution dropwise from a burette into the flask through which a beam of light passes. As soon as all of the KCN has been converted into the $KAg(CN)_2$ complex, the AgI begins to precipitate, producing the Tyndall effect.

The percentage of HCN and glucoside was then determined by Roe's formula:

$$\frac{0.0005404 \times \text{cc. } 0.01 \text{ N. } AgNO_3 \times 100}{\text{Dry weight of sample taken}} = \% \text{ HCN} \qquad (8)$$

The percentage of HCN thus obtained was multiplied by ten to obtain the approximate percentage of glucoside present.

Several checks were made under identical conditions and upon identical material, *i. e.*, material from the same flat, and material from different flats. In every case the variation in duplicate samples is less then 0.05% of glucoside.

RESULTS.

In preliminary assays it was found that an average of 1.618 per cent of glucoside was in the leaves of plants 4" high against 0.5192 per cent in the stems of the same plants.

(*a*) *Moisture.*—The relationship between the low moisture condition "A," the high moisture condition "B" and control condition "C" is shown in TABLE II and in Fig. 2 in which the percentage of glucoside is plotted against the growth period in days.

TABLE II.—(*a*) MOISTURE, PERCENTAGE OF GLUCOSIDE END OF FIRST WEEK.

	Set.	Series I.	Series II.	Series III.	Av. %.
L. M.	"A"	1.2200	1.2500	1.2250	1.2320
H. M.	"B"	0.8720	0.8250	0.8570	0.8510
Con.	"C"	1.4170	1.2350	1.2470	1.2990
		End of Second Week.			
L. M.	"A"	0.7575	0.7610	0.7590	0.7575
H. M.	"B"	0.9234	0.9195	0.9290	0.9240
Con.	"C"	0.5803	0.5730	0.5600	0.5711
		End of Third Week.			
L. M.	"A"	0.5370	0.5430	0.5560	0.5453
H. M.	"B"	0.6185	0.6340	0.6250	0.6258
Con.	"C"	0.5870	0.5950	0.6080	0.5966

(*b*) *Light.*—In the experiments with normal light and its effects on the glucosidal content three conditions of the plants are compared. In Fig. 3 the relationship between the low light condition, "D," the high light condition, "E," and the control condition, "C," is shown. Here again the percentage of glucoside is plotted against the length of time in days. The numerical results are shown in TABLE III. The difference in the amounts of light received by Sets "E" and "C" is discussed in the part of this paper which deals with the methods.

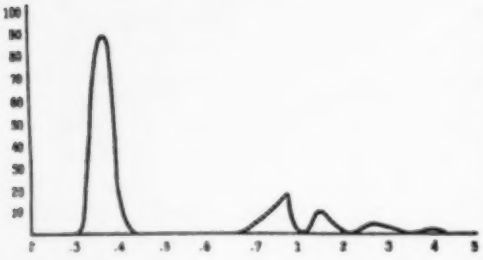

Fig. 1.—Transmission curve for Red Purple Ultra filter 5 mm. No. 597. The percentage of transmission is plotted against the wave-length.

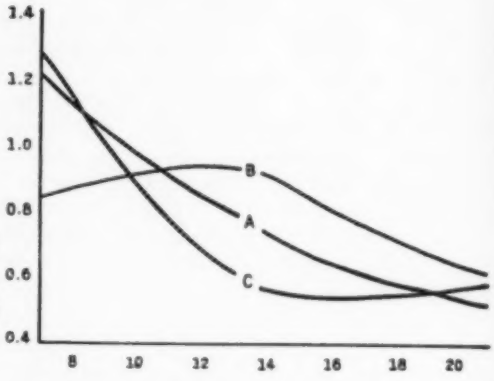

Fig. 2.—The effects of moisture variation on glucosidal content of flax. The percentage of glucoside is plotted against the time in days.

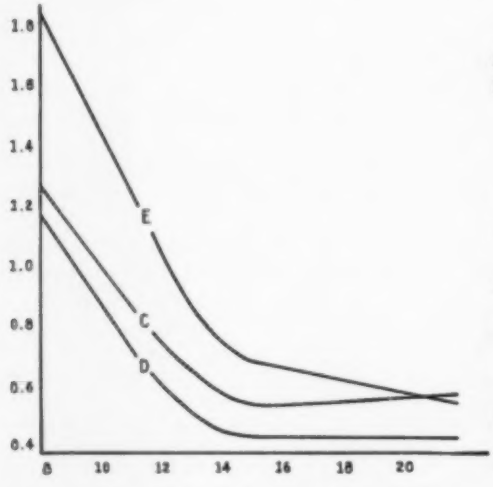

Fig. 3.—The effects of variations in light intensity on the glucosidal contents of flax. The percentage of glucoside is plotted against the length of time in days.

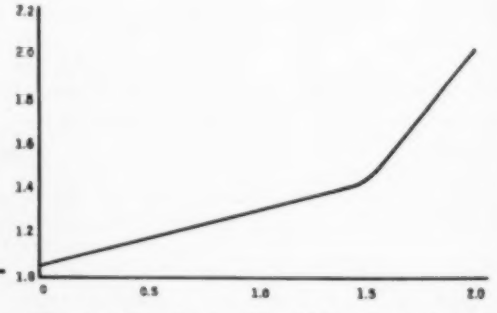

Fig. 4.—The rise in glucosidal content due to raying for various lengths of time. The percentage of glucoside is plotted against the raying time in hours.

TABLE III.—(*b*) NORMAL LIGHT, PERCENTAGE OF GLUCOSIDE END OF FIRST WEEK.

	Set.	Series I.	Series II.	Series III.	Av. %.
Con.	"C"	1.4170	1.2350	1.2470	1.2990
L. L.	"D"	1.1920	1.2320	1.2160	1.2133
H. L.	"E"	1.8700	1.9040	1.8380	1.8706
		End of Second Week.			
Con.	"C"	0.5803	0.5730	0.5600	0.5711
L. L.	"D"	0.4609	0.4813	1.4103	0.4508
H. L.	"E"	0.7102	0.7098	0.7123	0.7108

		End of Third Week.			
Con.	"C"	0.5870	0.5950	0.6080	0.5966
L. L.	"D"	0.4530	0.4740	0.4020	0.4430
H. L.	"E"	0.5710	0.5861	0.5790	0.5787

(*c*) *Artificial Light.*—The first experiment involving the use of artificial light, the results of which are given in TABLE IV, was undertaken to determine what possible effect raying, both during the daytime and at night, might have on the glucosidal content. It was also desired to see if any of the glucosidal material would disappear if the plants were kept in the dark for a number of days.

It was found that the flax plants which were rayed for two hours contained 2.62 per cent of glucoside on being assayed immediately after raying. A control set had 1.181 per cent of glucoside while the plants which were kept in the dark room contained only 0.684 per cent. The flat which was of the same age and grown under similar conditions to the three flats mentioned above was rayed for two hours during the night and assayed immediately after raying. The glucosidal content of this flat was 0.758 per cent.

The conditions of temperature and moisture were essentially the same throughout the experiment since the raying and assaying were performed within the same hour, in all of the flats except the one which was rayed at night.

TABLE IV.

Conditions of Plants.	Per Cent Glucoside.
Rayed for two hours during the daytime and assayed immediately after raying	2.62
Rayed the same night for two hours and assayed immediately after raying	0.758
Control set kept under the same conditions as set "C" described above and assayed at the same time as the first and fourth flats	1.181
Placed in the dark room and left there for two days. The plants were then cut in the dark room and assayed at the same time as the preceding flat	0.684

Considering the results obtained in the foregoing experiment with artificial light, it was thought advisable to see what effect several successive rayings would have upon the glucosidal content. For this experiment a single flat was used. One-half of it was rayed for two hours each night during the same number of nights. The plants were then allowed to remain in the greenhouse for twenty-four hours and were then assayed. It was found that very little difference in the glucosidal content resulted, the day-rayed plants containing 0.718 per cent while the night-rayed plants contained 0.688 per cent.

TABLE V.

Condition of Plants.	Per Cent Glucoside.
1/2 of a flat rayed two hours each day for 6 days. Assayed 24 hours after the last raying	0.718
The other half of the same flat rayed 2 hours each night for 6 nights. Assayed 18 hours after the last raying	0.688

Since the previous experiment undoubtedly indicated that the effect of raying on the glucosidal content of flax is somewhat temporary, from which the plant may recover if allowed to stand for a few hours, it became desirable to know what effect raying for various lengths of time would have on the glucosidal content. The curve representing the rise in glucosidal content with increased raying during the daytime, is indicated in Fig. 4. Here the plants were rayed for 0.5, 1.0, 1.5 and 2.0 hours and assayed immediately, beginning at 9 A.M. with the two-hour set and ending in the afternoon with the one-half hour set. The plants, although of different flats, were all of the same age (*i. e.*, twenty-one days old). They were grown under regular greenhouse conditions simulating those under which Set "C" was maintained. The raying time in hours is plotted against the percentage of glucoside found. TABLE VI serves as the basis for the graph.

TABLE VI.

Conditions of Plants.	Per Cent Glucoside.
No raying	1.050
Rayed for 0.5 hour	1.196
Rayed for 1.0 hour	1.300
Rayed for 1.5 hours	1.430
Rayed for 2.0 hours	2.030

Another experiment was carried out in which one flat, "C," grown under ordinary greenhouse conditions, and another flat, "A," grown under the same conditions but rayed for two hours, were cut immediately after the raying and the amount of glucoside hydrolysis determined at the end of 1, 2, 3, 4, 5, 18 and 25 hours. The results of this experiment are shown in TABLE VII. Here we see that the total glucoside formed in the rayed plants was 2.084% while that of the unrayed controls was 1.062%.

TABLE VII.

Assay Time in Hours.	% Glucoside Normal Set "C."	% Glucoside Rayed Set "A."
1	0.459	0.410
2	0.364	0.490
3	0.171	0.640
4	0.001	0.490
5	0.001	0.001
18	0.001	0.001
25	0.065	0.052
Total	1.062%	2.084%

DISCUSSION AND CONCLUSIONS.

The effect on the glucosidal content of flax produced by growth in a low moisture content soil, as can be seen in Fig. 2, has been generally that of reducing the amount of this substance. Although one point on the low moisture curve stands above that of the control set curve, it is believed that this difference is probably the exception rather than the rule. Flax plants, grown in a soil containing a high percentage of water, show a decided increase in the glucosidal content over the control condition. It is believed that at the time of the first assay on the plants, the effects of the various conditions had not yet become pronounced. It seems further possible that in the case of Set "B" the added water at first either caused an increased rate of translocation or increased the rate of secretion of enzyme as suggested by the work of Pickler (11), causing perhaps a subsequent decomposition of the glucoside.

Reynolds (12) has suggested that the glucoside in flax may possibly be produced largely in the actively growing cells and gives as evidence the fact that the percentage of glucoside decreases as the plants grow older and that the young tops of old flax plants contain almost as high a percentage of glucoside as do young plants. These facts, together with the fact that plants grown in a dry soil produce fewer new leaves, probably explain why the low soil-moisture set should give a low yield and the high soil-moisture set a high yield of glucoside. In the same paper Reynolds reported that healthy flax plants of a given age yielded 0.63% glucoside as against yellow plants (low soil-moisture growth) of the same age which yielded 0.083% glucoside. This certainly suggests that the percentage of moisture in the soil must affect the percentage of glucosides present in flax.

The reaction of the plants to a high light condition has been that of increasing the glucosidal content. In Fig. 3 we see that in the high light condition the plants show a high percentage of glucoside at the time of the first assay. This percentage decreases more or less regularly with the control "C." The fact that the low light curve "D," parallels the other two, suggests, no doubt, a relationship between these three conditions. Such results might be compared with the work of Eckerson (13) which suggests that low light conditions produce a retardation in the activity of reductase. If the glucoside-building mechanism, however, is stimulated by light, then we probably have an explanation for the results obtained under high light conditions

In the experiments in which artificial light was used it has been shown that long ultraviolet radiations are certainly efficacious in bringing about a variation in the glucosidal content of flax. In the plants rayed during the daytime the enzyme, linase, is probably stimulated in such a way as to build up more glucoside.

During the day a constant supply of carbohydrates plus the stimulation of nitrogen absorption, as demonstrated by Tottingham and Loswma (14), provide more favorable conditions for glucoside-synthesis than at night. During the night time ultraviolet light seems to invest the enzyme (linase) with added destructive powers. As for the constructive effects of ultraviolet light we have the work of Tottingham and Moore (15) who found a definite increase in protein, or in non-protein, non-lipide nitrogen in several economic plants under Vitaglass. There is also the work of Miss McCrea (2) which suggests a similar effect of light through Vitaglass on the seedlings of *Digitalis purpurea L.* The increase in glucosidal content reported by Miss McCrea, although contested by Arthur and Leonard (3) may be an actuality in view of the results reported here. The conditions of the drying process were not the same in the two experiments and it has been found by Hamilton (16) that great variations in chemical constitution exist in drugs under different conditions of light and temperature. Especially is this true of glucosidal drugs. There is also the factor of the time of harvesting, which, in the case of *Digitalis purpurea L.*, is a very important one. Miss McCrea collected her samples at the time of flowering which is accepted as the correct time for obtaining a high glucosidal-yielding drug. There was also the method of sampling to be considered. Arthur and Leonard used six plants from each group for analysis while Miss McCrea selected two samples from each group, each sample consisting of the leaves of 20 plants. In the latter experiment small differences of individual plants were ruled out because of the number of plants used in the assay.

It may well be that Miss McCrea's higher glucosidal values are associated with some such temporary factors as are demonstrated as important in the present work.

That the glucoside is decreased in quantity during the night raying and also during the two days in the dark room, a condition which would greatly reduce the labil carbohydrate content, is shown in TABLE IV. It was also found that the high or low glucosidal content of plants rayed over a period of days and nights, respectively, would, if the plants are allowed to recover for a few hours, return to a uniform percentage of glucoside. This suggests that the immediate effect of raying is a temporary one. These results are shown in TABLE V. In this connection it might be mentioned that Kerstan (17) in studying the physiological significance of the glucosides in several species of *Aesuclus* and *Salix* found an increase in the glucosidal content in the leaves during the daytime and a corresponding decrease at night-time in much the same way as the carbohydrates.

The quantitative effect of raying with ultraviolet is shown in TABLE VI. Here the percentage of glucoside seems to be proportionate to the length of raying time and probably indicates that the glucoside-producing mechanism is stimulated not only by the quality of light but also by the length of time it is applied. It is to be noted that in all of these ultraviolet experiments only the long ultraviolet irradiations from the lamp reached the plants.

The last experiment in which the HCN, calculated in terms of glucoside, liberated during 1, 2, 3, 4, 5, 18 and 25 hours from rayed and unrayed sets, was determined gives a further indication of the reactivity of the glucoside mechanism to ultraviolet irradiation. Although the hydrolysis took place somewhat more rapidly during the first hour from the unrayed set by the end of the third hour more HCN had been released from the rayed set and the total amount released was almost twice as much as from the unrayed set. The hydrolytic, as well as the synthetic reaction was stimulated by exposure of the plants to long wave ultraviolet.

SUMMARY.

(1) Several flats of flax were grown in a soil containing a low percentage of moisture. This condition produced a high dry-weight precentage but lowered the glucosidal content slightly from the control.

(2) Similar sets grown in a soil containing a high percentage of moisture showed a low dry-weight percentage and an increase in the percentage of glucoside over that of the control. This is possibly due to the fact that the glucoside-producing enzyme is secreted in greater quantities in plants under a high moisture condition.

There is also the fact that the glucoside is probably produced only in the actively functioning cells and since the leaves contain considerably more glucoside than that found in the stems and, furthermore, since the wet soil sets contained a considerably greater percentage of water, there was of necessity a greater number of actively functioning cells and consequently a higher percentage of glucoside.

(3) Plants grown in full light show a marked increase in the glucosidal content over those grown under low light conditions.

(4) Long ultraviolet radiations, when applied to plants during the daytime, invariably increased the percentage of glucoside. When applied at night the opposite or no effect was produced.

(*a*) The effect of the long ultraviolet, therefore, is apparently that of the activation of the glucoside-producing mechanism. This effect, however, is only a temporary one from which the plants may recover in a short period of time.

(*b*) It was further shown that the glucoside of flax largely disappears during forty-eight hours in the dark.

(*c*) The rate of decomposition of glucoside from rayed flax seems to differ somewhat from that of unrayed flax.

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"What is being done in hospital pharmacy to-day? Colleges of Pharmacy have recognized that real professional pharmacy is a necessary adjunct to every hospital and so have studied this problem. They also know that the real pharmacist must be trained in hospitals as well as in schools, and many schools have established this relationship and at the same time many hospitals have arranged internships for pharmacists. As a result, the American College of Surgeons in October 1936, adopted minimum standards for a hospital pharmacy. This will mean that soon every hospital must have a properly trained pharmacist and a well-equipped pharmacy, or secure pharmaceutical service from an *approved* pharmacy outside.

"The AMERICAN PHARMACEUTICAL ASSOCIATION has established a sub-section to study hospital needs from the pharmacist's standpoint, and the American Hospital Association has appointed a committee to study hospital pharmacy from the hospital's standpoint. These two committees are coöperating."—From Pharmacy Week Address of Edward Spease.

A COMPARISON OF THE PHARMACOLOGICAL SYNDROMES OF ERGOSTETRINE (ERGONOVINE) AND THE ERGOTOXINE GROUP OF ERGOT ALKALOIDS.*,[1]

BY MARVIN R. THOMPSON.[2]

The confusion resulting from the almost simultaneous appearance of reports from four different laboratories, announcing the discovery of what has been called the "true oxytocic principle of Ergot," has been clarified to a considerable extent. Although the principle was at first rather widely believed to be non-alkaloidal, the writer's original identification of the principle as an alkaloid (1), and his original contention (2) that the principles obtained in the four different laboratories were one and the same alkaloid has been acknowledged by the different groups of workers (3) after an exchange of specimens. The matter of selecting a single name for the new alkaloid has been at least partially settled. Because of the obvious difficulty of choosing one from the four assigned by the discoverers (ergostetrine (Thompson), ergometrine (Dudley and Moir), ergotocin (Kharash and Legault), ergobasine (Stoll and Burckhardt)), the Council on Pharmacy and Chemistry of the American Medical Association voted to adopt the name "ergonovine" for the new alkaloid (4), thus creating uniformity of nomenclature in the United States but not in other countries.

The total alkaloids of ergot may conveniently be classified according to differences in oxytocic activity, with the least toxic but most clinically active ergostetrine on the one hand, and the most toxic but clinically least active ergotoxine group of alkaloids (ergotoxine, ergotamine, sensibamine and ergoclavine) on the other. The members of the latter group are qualitatively indistinguishable in important pharmacodynamic actions and indeed apparently differ only slightly in these actions from the quantitative standpoint (5, 6). Although all five of the alkaloids have been used in these studies, the similar nature of the action of the four alkaloids comprising the "ergotoxine group" makes it unnecessary to reproduce illustrations and devote space to detailed considerations of all of the individual alkaloids. Since ergotoxine itself is typically representative of the four alkaloids comprising the group, it suffices to confine the experimental data and discussion to ergotoxine and ergostetrine for the purposes of this paper.

The ergostetrine used in these studies was the crystalline free base prepared by the author as described elsewhere (5). The ergotoxine employed was in the form of the crystalline ethanesulfonate, kindly supplied by Burroughs Welcome and Co. The ergotamine used was in the form of the crystalline tartrate, generously supplied by the Sandoz Chemical works. The ergoclavine was obtained as an ampulled solution through the courtesy of Dr. Joseph Rosin of Merck and Co., while the sensibamine employed consisted of the ampul solution manufactured by Parke, Davis and Co. and distributed commercially under the proprietary name "Ergone."

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* Scientific Section, A. PH. A. meeting, Dallas, Texas, August 1936.

[1] Presented at the Washington, D. C., meeting of the American Society for Pharmacology and Experimental Therapeutics, Mar. 1936; also at the Rochester, N. Y., meeting of the American Association for the Advancement of Science, June 1936.

[2] Emerson Professor of Pharmacology, School of Pharmacy, University of Maryland.

The ergotocin, ergometrine and ergobasine used in obtaining certain of the reproduced tracings consisted in all instances of authentic specimens of crystalline material obtained through exchanges with the three other groups responsible for the independent discovery of the variously named alkaloid.

BLOOD PRESSURE.

The effect of the ergotoxine group of alkaloids is well known. Single intraven-

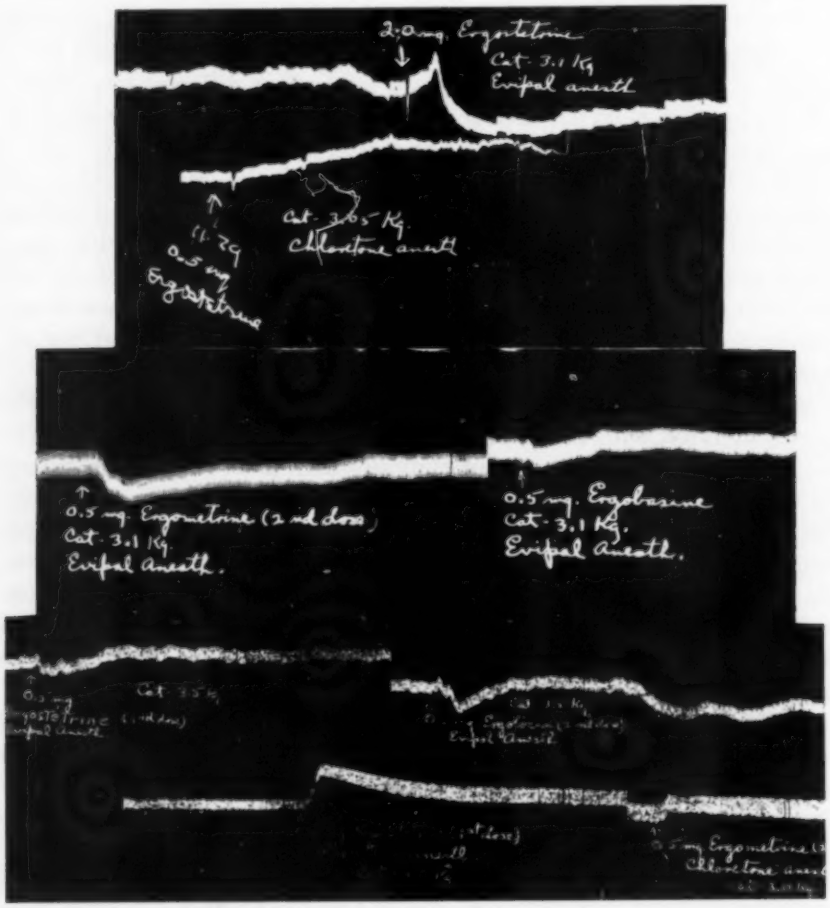

Fig. 1.—The carotid blood pressure effects of ergostetrine on cats anesthetized with chloretone and the barbiturate "evipal."

ous doses of 0.05 to 0.15 mg. per Kg. to anesthetized or unanesthetized cats or dogs produce a strong pressor action lasting for 15 to 60 minutes or more. The blood pressure returns to normal long before the drug has spent itself, as evidenced by the fact that repeated dosage results in progressively decreasing pressor response, leading to a reversal of the pressor action of epinephrine (the latter especially in cats). The literature deals extensively with these effects.

On blood pressure, ergostetrine differs considerably from the four alkaloids

comprising the ergotoxine group, although the difference is not such as to enable one to detect or estimate ergostetrine in admixture with the other alkaloids. The author (5) ascribed a relatively weak pressor action to ergostetrine, with the occasional observation of a depressor effect on cats anesthetized with chloretone. Davis, *et al.* (7), concluded that the same alkaloid has sometimes a demonstrable pressor action in pithed cats, but a depressor action in anesthetized animals. It appears, therefore, that there is a disagreement regarding the blood pressure action of ergostetrine.

This discrepancy is apparent, however, rather than real. Whether one obtains a pressor or a depressor response depends upon the type and depth of anesthesia. Figure 1 shows the depressor action on cats anesthetized with a barbiturate, and the pressor action on cats anesthetized with chloretone. The same illustration shows the progressively decreasing response following repeated doses.

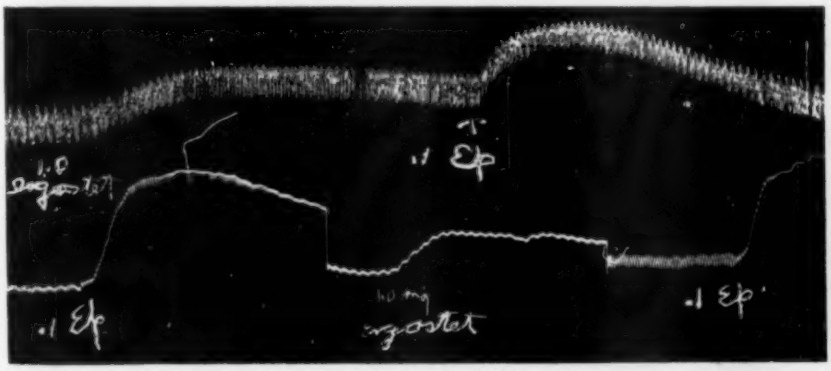

Fig. 2.—Showing the inability of ergostetrine to significantly influence the carotid blood pressure effect of epinephrine on a dog (upper tracing) and a cat (lower tacing), both anesthetized with chloretone.

Figure 2 shows the pressor action on a dog and cat, and the failure of ergostetrine to alter the pressor effect of epinephrine.

THE SITE AND CHARACTER OF THE ACTION OF ERGOSTETRINE AND THE ERGOTOXINE GROUP.

1. Isolated Rabbit Uterus.—That ergostetrine stimulates isolated segments of the mature rabbit uterus, in contrast to the depressing or paralyzing action of the ergotoxine group of alkaloids is already well established (5, 7, 8, 9, 10). Figure 3 is included merely to show the similarity of action of the four-named alkaloids now known to be one and the same alkaloid, and also to show how the presence of even relatively small amounts of the ergotoxine group in admixture with ergostetrine (as found in either aqueous or hydroalcoholic extracts) results in paralysis of the tissue so that the ergostetrine loses its effect in stimulating contractions. Preparations Nos. 42 and 43 in the last part of the tracing were solutions containing 0.15 mg. of ergostetrine and 0.15 mg. of ergotoxine activity (the latter by Broom-Clark assay) per cc. *For this reason, Ergot preparations containing ergostetrine, but free from the ergotoxine group, can be assayed on the isolated rabbit uterus, but the er-*

gostetrine activity of ergot preparations containing even small amounts of the ergotoxine group cannot be accurately estimated without prior chemical separation of the ergotoxine group. (Fig. 3.)

That ergostetrine is not wholly free from the depressant or paralyzing action characteristic of the ergotoxine group is shown in Fig. 4. This is important in connection with assaying ergostetrine on the rabbit uterus, emphasizing the necessity

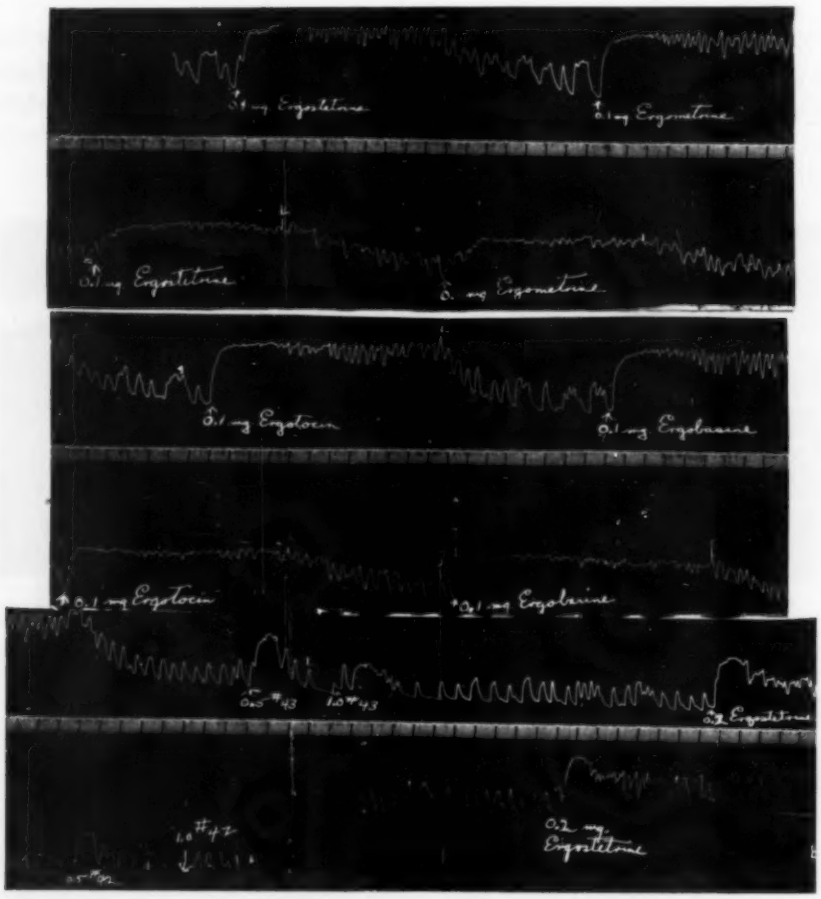

Fig. 3.—The stimulant effect of the new alkaloid on the isolated rabbit uterus, showing also the paralyzing effect of the ergotoxine-containing solutions Nos. 42 and 43.

of working with the smaller dose ranges to avoid a gradually developing paralysis from repeated doses which can significantly interfere with the quantitative accuracy of the method. (Fig. 4.)

From the foregoing, it would seem that ergostetrine produces its action by direct stimulation of sympathetic endings, since the sympathetic supply of the rabbit uterus is believed to be principally augmentor, and since the ergotoxine group can inhibit or abolish the stimulant action of either epinephrine or ergostetrine.

This explanation of the site and character of action is tenable if it is true, as widely believed, that the ergotoxine group acts exclusively upon the sympathetic endings. The latter has never been adequately proven, however, and it can be just as logically claimed, as far as the isolated rabbit uterus is concerned, that neither ergostetrine nor the ergotoxine group acts exclusively on the augmentor sympathetic endings

Fig. 4.—Showing how a large dose of ergostetrine produces first its characteristic stimulant effect on the isolated rabbit uterus, then distinct evidence of paralysis finally reaching such a degree as to almost abolish the action of 0.4 cc. epinephrine 1:10,000.

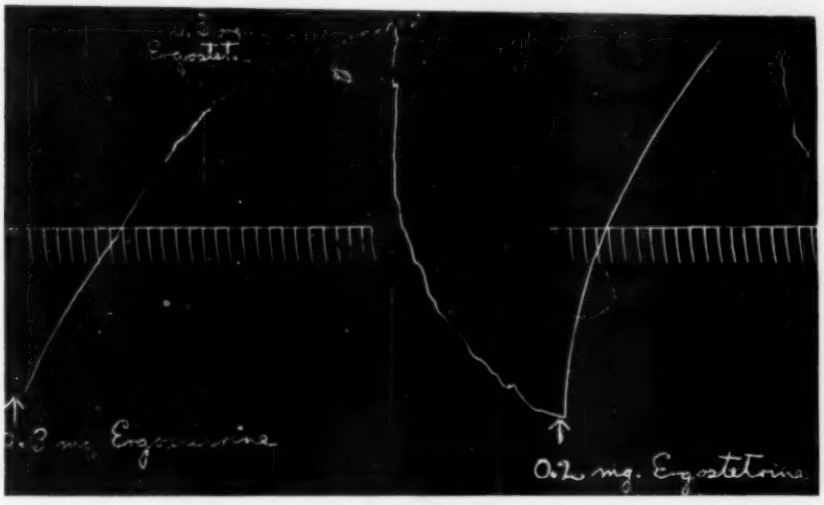

Fig. 5.—The strong contractions induced in the isolated uterus of an immature (250 Gm.) guinea pig. Note the complete absence of any epinephrine-like action.

but that all of these alkaloids act directly upon the uterine muscle to a considerable extent in addition to the sympathetic endings, ergostetrine acting by stimulation and the ergotoxine group by depression following effective dosage. The material which follows also has direct bearing upon the question.

2. *The Guinea-Pig Uterus.*—It is well known that epinephrine causes relaxation of the isolated guinea-pig uterus. This action is believed to result from a purely stimulant action on sympathetic endings which are inhibitory to the guinea-pig uterus (in contrast to the reverse situation in the rabbit).

If ergostetrine acts by stimulation of sympathetic endings, sparing the muscle itself, one should obtain relaxation of the guinea-pig uterus as in the case of epinephrine. Such, however, is not the case, as shown in Fig. 5, in which the uterus of an immature guinea pig (as specified by the U. S. P. for assaying Liquor Pituitarii Posterii) was used. Ergostetrine produced strong contractions, whereas epinephrine relaxes the same type of uterine muscle. It could be argued that the innervation of the guinea-pig uterus is not well developed in the sexually immature animal, thus accounting for the unexpected (?) results, but even if this were true, the fact that contractions were produced definitely argues for a direct action on the uterine muscle, or upon parasympathetic augmentor endings. (Fig. 5.)

But can ergostetrine action on inhibitory sympathetic endings also be demonstrated on the guinea-pig uterus? Figure 6 shows that it can. In this experiment,

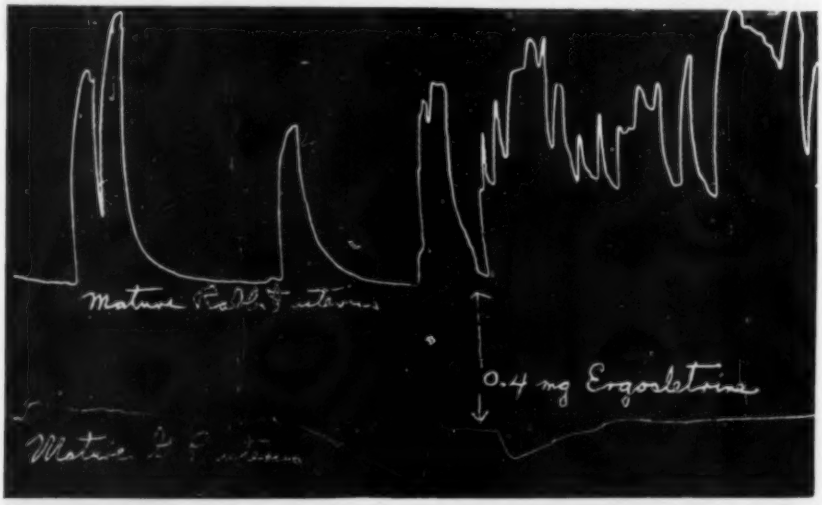

Fig. 6.—The effect of ergostetrine on the isolated rabbit uterus (upper tracing), and on the isolated mature guinea-pig uterus (lower tracing), the ergostetrine being administered to the guinea-pig uterus while in a state of contraction. Note the prompt relaxation followed by a return to the contracted state.

the uterus of a sexually mature guinea pig was used (lower tracing). It will be noted that as ergostetrine was administered, with the muscle in the contracted state, relaxation promptly followed, due presumably to stimulation of inhibitory sympathetic endings. It will also be noted, however, that the relaxation was soon followed by a return to the contracted condition, due, it is believed, either to a stimulant action directly on the muscle, or upon parasympathetic augmentor endings. (Fig. 6.)

It is again apparent, therefore, that a stimulant action on another site, as well as on the sympathetic endings, can be experimentally demonstrated on the guinea-pig uterus. (See also Fig. 8 under action on intestine.) On both the guinea-pig and rabbit uterus, the ergotoxine group of alkaloids shows an action somewhat related to that of ergostetrine. The action of ergostetrine is apparently predominantly stimulant, very gradually giving way to a feeble paralyzing action. In marked

contrast, the action of the ergotoxine group is characterized by an initial stimulation which rapidly gives way to a depressant or paralyzant action. The above is demonstrable especially in large doses, the action on the nerve endings probably predominating in concentrations comparable to therapeutic doses.

3. Islated Guinea-Pig and Rabbit Intestine.—It is also possible to demonstrate the dual nature of ergostetrine action on both the guinea-pig and rabbit intestine. Figure 7 represents two sections of a continuous tracing in which isolated segments of the uterus and intestine of a sexually mature guinea pig were made to record their respective movements simultaneously. The uterine action has already been

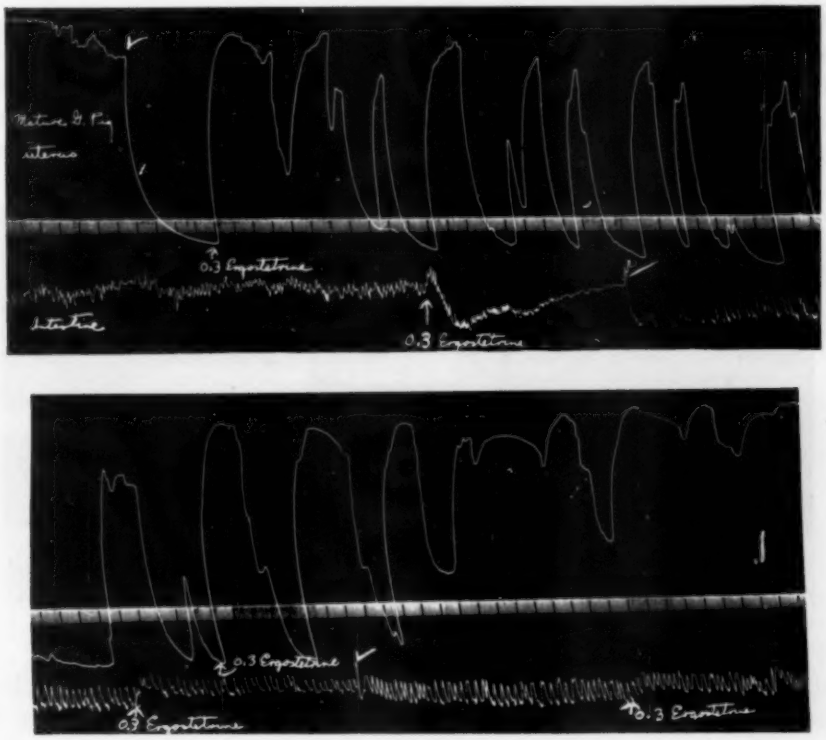

Fig. 7.—Two sections of a continuous tracing of an isolated segment of a mature guinea-pig uterus (upper tracing) and a segment of intestine from the same guinea pig (lower tracing). Fifty-cc. tissue chambers were used in all of the isolated tissue work.

dealt with, but it can again be noted in Fig. 7 that, with the ergostetrine administered to the uterus in the relaxed condition, the sympathetic inhibition is not in evidence (as would be expected), but the indication of the direct stimulant action on the smooth muscle (or parasympathetic augmentors) is strikingly present. Turning to the tracing of the intestinal movements in Fig. 7, one obtains still further evidence of the dual nature of the action. As one would expect, the first application of ergostetrine caused inhibition of the intestinal movements (presumably due to sympathetic stimulation), promptly followed by an increase in tonus before the drug was removed (presumably due to the direct muscle or parasympathetic

stimulation). After washing out the drug, relaxation followed (as one would expect from the removal of a drug having both types of action).

In working with guinea-pig intestine, it was observed that the sympathetic endings are rather easily paralyzed by all of the ergot alkaloids. It can be noted in Fig. 7 that although the first dose of ergostetrine (purposely rather large) produced inhibition, the second and third doses did not, but produced, instead, an increase in tonus. It is believed that this phenomenon is best explained by assuming that the first dose of ergostetrine produced the expected sympathetic inhibition, but that this dose was large enough to paralyze the endings to such an extent that the subsequent doses could exert only a direct stimulant action on the muscle, or upon parasympathetic endings, causing the tonus increase without the preliminary sympathetic inhibition. (Fig. 7.)

Figure 8 shows the rabbit intestine to be similarly affected by ergostetrine. Here, however, the sympathetic endings seem strikingly less subject to paralysis than in the case of the guinea-pig intestine. The prompt relaxation due to sym-

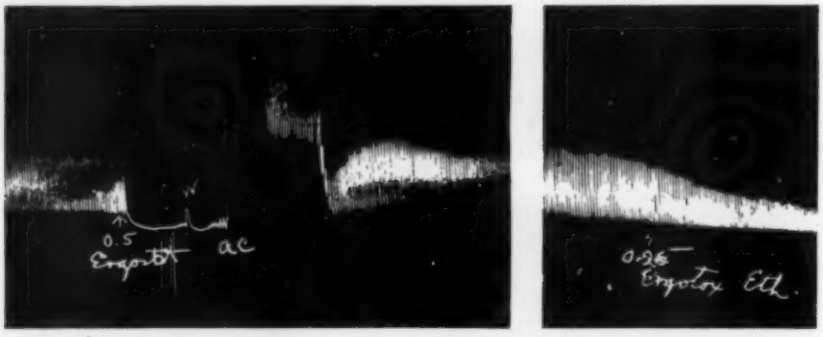

Fig. 8.—Isolated rabbit intestine. Showing the effect of ergostetrine and ergotoxine in inhibiting the rhythmical movements. Following ergostetrine, recovery was hastened with acetyl-choline.

pathetic stimulation is again characteristic. The ergotoxine group of alkaloids acts in a somewhat similar direction on the intestine, but the stimulant action is weaker and the paralyzing action much more powerful on the nerve endings in effective doses, than in the case of ergostetrine. The same is true for the action on the uterus. The direct muscle or parasympathetic stimulation (tonus increase after the sympathetic inhibition) can again be made to come into evidence on the rabbit intestine, especially from the larger dose levels. (Fig. 8.)

The foregoing experiments have a definite significance in pharmacodynamic analysis of action. But it must be recognized that this significance is beset with certain limitations in predicting therapeutic parallels particularly in the matter of dosage or effective concentrations of the various alkaloids.

The results from isolated tissues and separate physiological functions quite naturally give rise to the question: What happens to the key functions of the intact animal body when therapeutically effective and sub-toxic or even toxic doses enter the circulation? It is extremely difficult to obtain a satisfactory answer to this question, since, in order to obtain a direct record of the behavior of the various

"key" organs and functions, simultaneously taken, the otherwise intact animal body must necessarily be subjected to anesthesia as a complicating factor. This, if nothing else, probably at least partially interferes with effects which might be otherwise reflexly induced, and probably interferes to some extent with the direct actions. However, most of the published evidence of the action of the ergotoxine group has been obtained from anesthetized or pithed animals, and the results similarly obtained with ergostetrine are of definite importance from the comparative pharmacological standpoint.

The Actions of Ergostetrine and the Ergotoxine Group on the Anesthetized Dog.—Because the innervation of the uterus in the dog apparently qualitatively approximates that of the human and because the use of a relatively large experimental animal would offer obvious advantages, the dog was selected for the experiments to be included in the present paper.

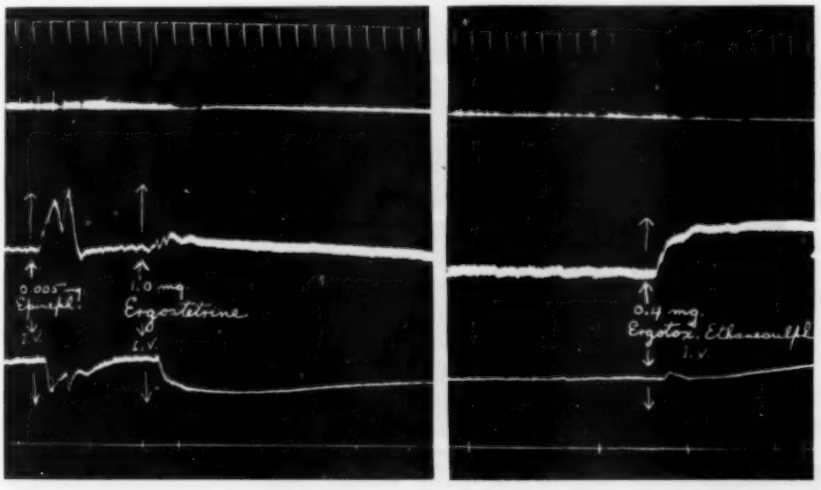

Fig. 9.—Dog, 10.5 Kg.; evipal anesthesia. Tracings top to bottom, time in minutes, respiration, carotid blood pressure, kidney volume and urine excretions from the ureters. Forty-five minutes of the tracing omitted between the two sections.

Anesthesia was induced and maintained at a rather light level (corneal reflex always present) with the barbiturate "Evipal," administered intravenously as required. Figure 9 represents a continuous tracing of time in minutes, respiration, carotid blood pressure, kidney volume and urine output (total uniform drops directly from both ureters), from a female dog weighing 10.5 Kg. The rather large dose of 1.0 mg. of ergostetrine, given intravenously, produced a depression or respiration, an almost negligible effect upon carotid blood pressure, an increased amplitude of the heart-beat, a great decrease in kidney volume, and a complete checking of urine excretion. At the end of approximately an hour, the various functions again approached the normal. The comparative effects of the ergotoxine group are then shown. Because of the much greater toxicity of the ergotoxine group, the smaller dose of 0.4 mg. of ergotoxine ethanesulfonate (U. S. P.) was given intravenously. The respiration, blood pressure and heart action are qualitatively similar to those of ergostetrine, but quantitatively the action of ergotoxine is much stronger even in less than half the dosage. The ergotoxine effects on kidney volume and urine output were strikingly different from the ergostetrine effects. The effect of ergotoxine on kidney volume was slight as compared with ergostetrine, and was increased instead of decreased. This difference is also reflected

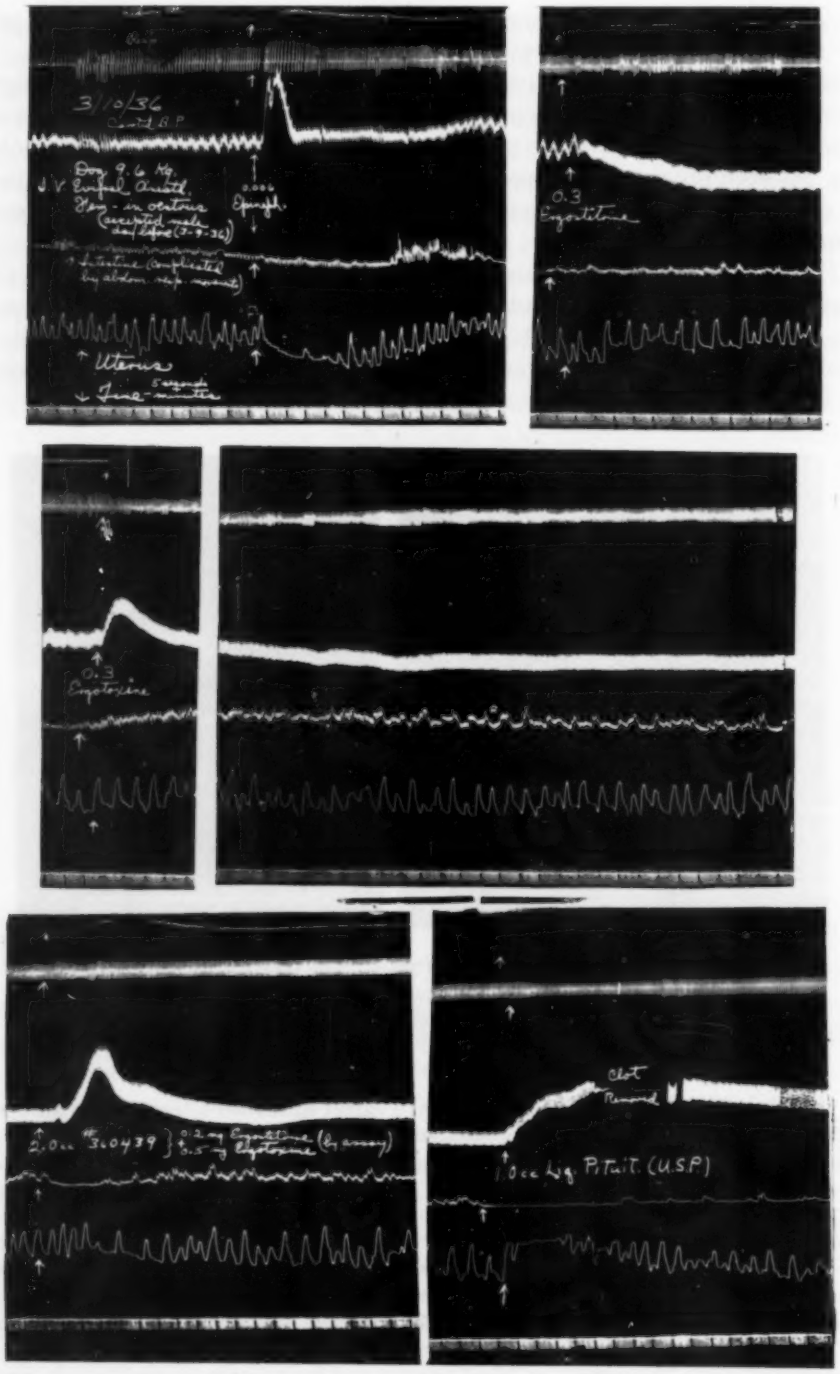

Fig. 10.—Continuous tracing in six sections. Five minutes of tracing cut out between Sections 1 and 2, forty minutes from between 2 and 3, five minutes from between 3 and 4, twenty minutes from between 4 and 5 and thirty minutes from between 5 and 6.

in urine excretion, which, instead of being decreased or checked, was definitely increased. The ergotoxine effects may have been complicated by the initial ergostetrine dose, even though there was a lapse of an hour between doses (Fig. 9).

Figure 10 represents a similar experiment, but upon a female dog definitely in œstrus (accepted a male the day before the experiment). In this experiment, kidney volume, respiration, carotid blood pressure, intestinal movements, uterine movements and time in 5-second and minute intervals are recorded. The dog weighed 9.6 Kg. and intravenous evipal anesthesia was used as in Fig. 9. The effects of an intravenous dose of 0.3 mg. of both ergostetrine and ergotoxine ethanesulfonate are recorded for comparison. The tracing of the intestinal movements is complicated by respiratory movements, and must, therefore, be interpreted with caution. The effects of epinephrine and posterior pituitary are included to aid in the interpretation of the actions of the ergot alkaloids. (Fig. 10.) The effects produced are, in the main, in agreement with those in Fig. 9. It is interesting to note in this animal, however, that epinephrine produced a transitory relaxation of the uterus, while ergostetrine, ergotoxine and posterior pituitary produced a definite increase in tonus. It appears certain, therefore, that ergostetrine and ergotoxine exert their oxytocic action through a site other than the sympathetic endings stimulated by epinephrine, just as in the case of posterior pituitary. It does not necessarily follow that this other site would have to be the smooth muscle directly (the mechanism through which posterior pituitary is supposed to act). But from present understanding, one must necessarily conclude that this other site would have to be either (1) the smooth muscle directly, (2) parasympathetic endings (which could conceivably become augmentor in function during œstrus or pregnancy, with a corresponding reverse in the normal function of the sympathetics) or (3), a mechanism as yet unknown. After noting the positive evidence of significant sympathetic stimulation in normal, unanesthetized animals (mydriasis anger, etc.) one is inclined to believe that sympathetic stimulation must enter into the uterine action and yet, these other evidences of sympathetic stimulation (from rather large doses) may conceivably be due to an exaggerated liberation of epineprine from the adrenals as pointed out by Brown and Dale (8). Smaller doses of the alkaloids, as used in the anesthetized dog experiments, may not call forth enough epinephrine from the adrenals to complicate the action of the ergot alkaloids on the uterus. This hypothesis receives support from the effects produced by the larger dose of ergot alkaloids given in the form of solution No. 360439. Here some evidence of sympathetic stimulation (from elaborated epinephrine?) appears in both the intestinal and uterine effects. Nevertheless, results to date do not furnish a clear and indisputable answer to the question. It appears that the ergot alkaloids must certainly produce a part of their effects by an action on a site other than the sympathetic endings stimulated by epinephrine. The study is being continued.

SUMMARY.

The site and character of the pharmacological action of ergostetrine and the ergotoxine group of ergot alkaloids has been comparatively studied; *first*, on the various types of isolated smooth muscle normally innervated by the sympathetic and parasympathetic branches of the autonomic nervous system, and, *second*, upon autonomically controlled functions of anesthetized intact dogs.

CONCLUSIONS.

1. Evidence has been obtained which strongly indicates that the pharmacodynamic action of both ergostetrine and the ergotoxine group of ergot alkaloids is not confined to the sympathetic endings stimulated by epinephrine.

2. The character of the action of ergostetrine differs from that of the ergotoxine group of alkaloids in that the action of ergostetrine is predominantly stimulating, with only relatively feeble and delayed manifestations of a slowly developing paralyzing action, while the action of the ergotoxine group of alkaloids is characterized by a relatively weak initial stimulant action which rapidly gives way to a depressant paralyzing action, the stronger paralyzing action of the ergotoxine group undoubtedly accounting for the much greater toxicity characteristic of this group as compared with ergostetrine.

3. The clinically employed doses of 0.2 to 0.6 mg. of ergostetrine, or 0.5 to 1.5 mg. of members of the ergotoxine group, are not sufficiently large to call forth appreciable actions of the respective syndromes other than the oxytocic action, unless the larger dose ranges are administered too frequently over a period of time. It is believed that the spectacular effectiveness of ergostetrine as an oxytocic on either the ante-partum or post-partum uterus, or the uterus in the period of œstrus, of humans is due to a definitely increased irritability or responsiveness to the drug during those periods, thus making it possible for these small doses to produce a wholly satisfactory quantity and quality of oxytocic action without producing objectionable degrees of "side effects" or other actions of the syndrome.

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POSTGRADUATE OF PUBLIC AND INDUSTRIAL OFFICIALS.

Sir Richard Livingstone, president of Corpus Christi College, Oxford, comes foreward with the suggestion that there be established a form of supervised re-education of public and industrial officials. He holds that these should keep abreast of the times by giving them an opportunity to attend school periodically on the supposition that the education of a generation ago is by no means automatically adaptable to the needs of a rapidly changing world.

The Littauer foundation, designed to improve public administrations, is working along these lines. It is contended that all the learned professions should endeavor to keep up with the latest discoveries through regular convocations in their respective fields. It is stated that the re-education of public officials would pay dividends far in excess of the costs.

IT CAN BE DONE, SERIES NO. 12.*

BY J. LEON LASCOFF.

INTRODUCTORY.

The author stated he was glad to conduct the Prescription Clinic at this time and referred to the series he had conducted. The first series was presented at the Baltimore meeting, when he was requested to continue the work, and was also invited to deliver similar talks by other associations. These were delivered as follows:

Series No. 2, before the Massachusetts Pharmaceutical Association; No. 3, before Baltimore Branch, A. PH. A.; No. 4, before Maryland Pharmaceutical Association; No. 5, before Philadelphia Branch, A. PH. A.; No. 6, before New Jersey Branch and Rutgers University College of Pharmacy; No. 7, at the Dallas meeting, A. PH. A.; No. 8, before Iowa Pharmaceutical Association; No. 9, before Pittsburgh College of Pharmacy; No. 10, at the Connecticut Pharmaceutical Association; No. 11, before Ohio Pharmaceutical Association, Toledo; and No. 12, the presentation before the AMERICAN PHARMACEUTICAL ASSOCIATION at the New York meeting. The author, in introducing his subject, stated:

"It is of the greatest importance that prescriptions, like Galenicals, be of uniform appearance, whether put up in one pharmacy or another. For this reason, we have the U. S. P. and N. F. standards for preparations. Formerly, a prescription put up in different pharmacies varied in taste, color and appearance. I have made a study of this and have decided that there must be uniformity."

Some time ago the author spoke of the abuse of the "Shake Label." All too often, the careless dispenser makes this his great salvation (in his own mind) with the explanation, "I filled it exactly as the Doctor wrote it." Recently a pharmacist in Washington did this, and the patient became very ill. As a result, the pharmacist was forced to pay the expense of a costly lawsuit. The author continued:

"If any changes are made in a prescription, the physician *must* be consulted first; this applies to doses as well. If a physician prescribes an incorrect dose, it is the pharmacist's duty to notify him immediately. Otherwise, the physician may go on prescribing the wrong amount. If a physician is not consulted about the changes in a prescription, he will prescribe again in the original manner and, if the prescription is filled as written, the finished product will differ from the first mixture." The speaker stated that some of the prescription problems which he would present had occurred in the Lascoff pharmacy and others in pharmacies in other sections. He had experimented with them and would try to convince the hearers of the value of this experimental work. Comparison of samples No. 1 and No. 2 of these examples will reveal marked differences.

℞ 1	Sodium Bicarbonate	gr. XII
	Atophan	gr. V
	Acetphenetidin	gr. III *ss*
	Acetylsalicylic Acid	gr. IV *ss*
	Codeine Sulfate	gr. 1/8
	M. F. powders.	

* Section on Practical Pharmacy and Dispensing, A. PH. A., New York meeting, 1937.

The powders will not become pasty or caked if the prescription is compounded as follows: In an absolutely *dry* mortar, triturate the sodium bicarbonate, atophan and acetphenetidin together with 3 grains of sugar of milk for each powder. In a separate mortar which also *must be absolutely dry*, triturate the codeine sulfate and acetylsalicylic acid together with heavy magnesium oxide, 5 grains for each powder. Finally, mix the two lightly but thoroughly. As an added precaution, dispense in glassine or wax powder papers, the ends of which should be closed.

℞ 2	Tr. Belladonna	f℥ *ss*
	Citrate Potash	℥ I
	Tr. Hyoscyamus	f℥ II
	Water, *q. s.*	f℥ IV
	M. ft. Sol.	

This formula should be compounded as follows: Dissolve the potassium citrate in part of the distilled water. In a separate mortar, make a mucilage with 2 drachms of acacia, and add the solution to this. Mix the tinctures with the remainder of the water, and add this to the mucilage. The finished product will be a homogeneous mixture *without any separation.*

℞ 3	Acid Carbolic	gtt X
	Liq. Carbonis Detergens	f℥ II
	Acid Boric	℥ II
	Ung. Aquaphor	℥ I
	Aq. Font.	f℥ VI

The following procedure should be used in compounding the above: Rub the boric acid with six drachms of aquaphor. Dissolve the phenol in the water and incorporate in the aquaphor. Add the liquor carbonis detergens and a separation will be noted. Incorporating 2 drachms of liquid petrolatum results in a smooth, homogeneous ointment with no signs of separation.

℞ 4	Sodium Nitrite		
	Potassium Sulphocyanate	*aa*	gr. XXX
	Elixir Sodium Bromide		f℥ II
	Aqua Dist., *q. s.*		f℥ IV

This mixture should be compounded as follows: Dissolve the sodium nitrite in 1 ounce of distilled water. Dissolve the required amount of sodium bromide necessary to make a fresh elixir of sodium bromide in 1 ounce of distilled water. Dissolve the potassium sulphocyanate in 1 ounce of distilled water. In other words, dissolve all the ingredients separately. Add the simple elixir (necessary to make the elixir sodium bromide) and enough water to make four ounces. The elixir sodium bromide *must be freshly made.* It is advisable to dispense this 4-ounce mixture in a 6-ounce bottle. If the prescription is compounded as above no explosion will occur.

℞ 5	Bismuth Subgallate	℥ I
	Balsam Peru	℥ I
	Icthyol	♏ XL
	Benzoinated Lard	℥ IV

If compounded as written, this ointment will become gritty and a separation will occur. The following is the proper way to compound this: Rub the bismuth subgallate with 2 drachms of castor oil and 1 ounce of balsam peru. Add 2 ounces of benzoinated lard and mix gently. Mix the ichthyol with 1 ounce of benzoinated lard to make an icthyol ointment. Mix the two compounds and add the balance of the benzoinated lard. Keep in a cool place. If compounded as above, the result will be a smooth ointment with no signs of separation.

℞ 6	Phenol	2.0
	Tincture of Iron Chloride	15.0
	Adrenalin Chloride	4.0
	Tincture of Aconite	8.0
	Glycerin	30.0
	Glycothymoline, *q. s.*	120.0

When this compound is made up as written, a strong effervescence occurs which will blow the stopper from the bottle and cause the loss of part of the material. The trouble-maker here is the tincture of ferric chloride. As this is acid in reaction, it reacts with the glycothymoline, which is alkaline, and causes the effervescence and a precipitate of ferric hydroxide. Furthermore, adrenalin is decomposed by both alkalies and iron salts. The solution to the problem is one of the most interesting I have come across. As noted by the following comparison, the content of solution of ferric chloride is exactly the same in both tincture of ferric chloride and tincture of ferric citrochloride. The main difference between the two is the addition of sodium citrate (which is alkaline) to the tincture of ferric citrochloride.

Tr. Ferric Chloride.		Tr. Ferri Citrochloride.	
Solution Ferric Chloride	350 cc.	Solution Ferric Chloride	350 cc.
Alcohol to make	1000 cc.	Sodium Citrate	450 Gm.
		Alcohol	150 cc.
		Water to make	1000 cc.

Of course the pharmacist has no right to replace the glycothymoline with anything else, but, if in place of the tincture of ferric chloride, tincture of ferric citrochloride is used, the final product becomes a clear mixture with no trace of precipitation or change of color. The sample I have experimented with has now been standing for some weeks and looks exactly the same as when first compounded. Whether or not the adrenalin will decompose on standing, is a matter of debate. The pharmacist should discuss this matter with the physician, with a view toward removing this possibility.

℞ 7	Menthol	0.3
	Spiritus Vini Rect.	12.0
	Phenol	1.2
	Calamine	8.0
	Zinc Oxide	4.0
	Pulv. Camphor	8.0
	Aqua Hammamelidis *ad*	180.0

The difficulty in the above lies in the fact that there is not sufficient alcohol to keep the camphor and menthol in solution. The addition of 30 grains of tragacanth, making a smooth paste with the hammamelis water and adding the camphor and menthol previously triturated to a liquid, forms a smooth mixture, which shows no separation or lumpiness on standing.

℞ 8	Iron and Ammonium Citrate U. S. P. XI	ʒ III
	Syrup Orange	ʒ I
	Distilled Water, *q. s.*	ʒ VI

Iron and ammonium citrate in solution becomes alkaline on standing. Syrup of orange containing citric acid is sufficiently acid in reaction to cause the formation of gas, which burst the bottle. The British Pharmacopœia gives a formula for syrup orange without citric acid, in proportion of tincture of orange, 1 part in 8 parts of syrup. When this is used, effervescence will not occur, and there will be no difficulty.

℞ 9	Quinine and Urea Hydrochloride	0.6
	Mercury Salicylate	3.0
	Lanolin	1.0 Add to
	Olive Oil	30.0 the water

In the above formula, the quinine and urea hydrochloride will not dissolve in the olive oil, and therefore the mixture will not be uniform. The best way to compound it is as follows. Dissolve the quinine and urea hydrochloride in a few drops of water. Emulsify with the lanolin, then add the mercury salicylate, rubbing well with the olive oil.

℞ 10	Morphine Sulfate	gr. IV
	Flexible Collodion, *q. s. ad*	℥ I

Morphine sulfate will not dissolve in the flexible collodion. It is therefore necessary to use morphine alkaloid. Dissolve the morphine alkaloid in about 1 drachm of alcohol. To this

solution, add the flexible collodion. The flexible collodion is miscible with the alcohol, and a perfect solution is obtained.

℞ 11	Boric Acid	ʒ II
	Zinc Oxide	ʒ II
	Ichthyol	10%
	Carbolic Acid	1/2%
	Petrolatum Liquid *ad*	ʒ IV

The addition of stearic acid will aid greatly in forming a non-separating liquid.

℞ 12	Cignolin	1/10%
	Acid Salicylic	ʒ I
	Ol. Amygd. Dulc.	fʒ II

Heat the oil with salicylic acid and cignolin. A clear solution is obtained, which, however, may precipitate. The addition of 10% castor oil will prevent this precipitation.

℞ 13 Acid Salicylic 1%, 2%, 3%, 4%, 5% in Sesame Oil

Salicylic acid is not as soluble in sesame oil as in castor oil. The addition of 10% castor oil will help to make a perfect solution.

℞ 14	Acid Salicylic	3.6
	Sulfur Præcip.	7.2
	Zinc Oxide	
	Talc	
	Glycerin *aa*	20.0
	Water *ad*	120.0

The addition of 35% to 50% of alcohol to replace that quantity of water will prevent the salicyclic acid from being thrown out of solution.

℞ 15	Balsam of Peru	
	Carron Oil	Each 22 parts

The addition of castor oil is necessary to make a homogeneous mixture.

℞ 16	Thigenol	4.0
	Resorcin	1.2
	Acid Salicylic	2.0
	Zinc Oxide	
	Calamine *aa*	8.0
	Glycerin	12.0
	Lime Water	16.0
	Rosé Water *ad*	120.0

Make a mucilage with about 15 grains of tragacanth in which triturate the resorcin and salicylic acid until completely suspended. Mix the zinc oxide and calamine together. To this add the glycerin and lime water. Rub the thigenol (like ichthyol) with 50 cc. rose water. Mix with calamine mixture. Lastly add enough rose water to make 120 cc.

℞ 17 Iodine 40% in Ol. Sesame

The iodine is to be triturated with the oil of sesame, previously warmed. Transfer to a glass-stoppered bottle and allow to stand for a few days with frequent agitation. The result should be an iodized oil equivalent in iodine content to the U. S. P. preparation.

℞ 18	Chloral Hydrate	ʒ IV
	Sodium Bromide	ʒ I
	Aromatic Elixir, *q. s. ad*	ʒ IV

Use low alcoholic elixir.

℞ 19	Copper Citrate	gr. 1/40
	Iron and Ammonium Citrate	gr. 10
	Syrup of Orange	f℥ *ss*
	Distilled Water *ad*	f℥ I
	Make 23 doses.	

Copper citrate is not soluble in water. In order to dissolve the copper citrate in the above formula, it is necessary to triturate it with about 15 grains of citric acid. More may be added if necessary. Separately dissolve the iron and ammonium citrate in the balance of the water, and add to the first solution. Lastly, add the syrup of orange. In the finished product, there will be an equal subdivision of doses of the copper citrate.

℞ 20	Ephedrine Sulfate	0.18
	Terpin Hydrate	3.00
	Elixir Phenobarbital, *q. s. ad*	60.00

If compounded as written, the terpin hydrate will remain undissolved, due to the fact that there is not sufficient alcohol.

A.

Triturate the terpin hydrate with about 3 Gm. of acacia, previously made into a mucilage with a small quantity of water. Add part of the elixir phenobarbital. Separately, dissolve the ephedrine sulfate in a few drops of water and add to the first solution. Lastly, add sufficient of the elixir to make the desired quantity.

B.

Obtain permission from the physician to compound the prescription as follows: Inasmuch as the terpin hydrate is soluble in 13 parts of alcohol, dissolve the terpin hydrate in 39 cc. of alcohol. In this solution, dissolve the ephedrine alkaloid. Now, in order to make up the lost quantity of phenobarbital, it will be necessary to add 2 1/2 grains of phenobarbital alkaloid. The finished product will be perfectly clear. In my opinion, this is the best way to dispense this prescription.

℞ 21	Phenobarbital	gr. 3/4
	Sodium Nitrite	gr. I
	Thyroid	gr. 1/4
	Aspirin	gr. V
	D. T. D. Caps. No. 24.	

Triturate the phenobarbital together with the thyroid and aspirin. Separately, triturate the sodium nitrite with about 12 grains of magnesium oxide, heavy. Mix both triturations and dispense in a screw-cap vial. The mortar and pestle must be perfectly dry and the capsules must be filled very quickly to avoid the absorption, by the powder, of moisture from the air.

℞ 22	Spirit of Ethyl Nitrite	℥ II
	Sodium Salicylate	gr. XXX
	Elixir Amidopyrine	f℥ IV
	Aquæ	f℥ IV
	Syrup of Tolu, *q. s. ad*	f℥ II

When the above is compounded, a color change is noted because of the well-known incompatibility of Spirit of Ethyl Nitrite with sodium salicylate and more so with amidopyrine which is a derivative of antipyrine. Because of this reaction and the constant opening of the bottle, to administer doses of the medicine, there is not much ethyl nitrite left after a while. The attention of the physician should be called to this fact and his permission to use spirit of ether instead of spirit of ethyl nitrite solicited.

℞ 23	Codeine Sulfate	gr. 1/4
	Extract Belladonna	gr. 1/6
	Ammonium Carbonate	gr. II
	Acid Acetylsalicylic	gr. III
	Ft. Cap. No. 1. Disp. Cap. No. 24.	

The problem in this prescription is to prevent liquefaction. The acid acetylsalicylic was tested for free acid, and found to contain but 1/1000% and 1/1500 moisture. The ammonium carbonate was triturated to a very fine powder and added to the compound last, without any more trituration. Upon experimenting I found that magnesium oxide, heavy, would not help in keeping the capsules dry. I also used kaolin with little success. I decided that the best manner of compounding would be to make a capsule of the ammonium carbonate (using a No. 5 capsule). Make another capsule of the codeine sulfate, extract of belladonna and the acid acetylsalicylic. Leave sufficient space in the capsule to permit placing the No. 5 capsule with the ammonium carbonate in it. In my opinion, this is the best way to prevent the ammonium carbonate from coming in contact with the other ingredients.

℞ 24	Creosote	ʒ I
	Ol. Eucalyptus	fʒ I
	Ol. Pini Sylvestris	fʒ I
	Compound Tincture of Benzoin	fʒ V
	Lac Magnesia, *q. s. ad*	fʒ II

The following procedure should be used in compounding the above: To a mucilage consisting of about 10 grains of tragacanth with a small quantity of water, add the compound tincture of benzoin, the oils and the creosote. Lastly, add the milk of magnesia, little by little, with constant trituration. The finished product will be a uniform homogeneous mixture without any separation.

℞ 25 Aluminum c Lanolin 25%
(Special Base)

The physician requested that the above be compounded with a special base, and that if a base other than lanolin would be more suitable, it should be used. On display here may be seen the prescription compounded with lanolin and one in which protegin was used. Protegin is a cholesterinized base which enables one to turn out very fine ointments, where ordinary bases are unsuitable.

℞ 26	Crude Coal Tar		fʒ I *ss*
	Zinc Oxide		
	Amylum	*aa*	ʒ III
	Nivea Cream, *q. s. ad*		ʒ IV

The Nivea Cream contains water. When this is mixed with the other ingredients, including the coal tar, the water of the cream will separate out. The proper method to employ is to dissolve the crude coal tar in a small quantity of carbon tetrachloride. Rub the zinc oxide and amylum with the Nivea Cream. Add to the coal tar. If the water separates, add a small quantity of aquaphor (also manufactured by the Duke Laboratories). This will absorb the water. If aquaphor is not available, use anhydrous lanolin or some other suitable absorbing agent.

℞ 27	Castor Oil		
	Spirit of Turpentine		
	Stronger Ammonia Water	*aa q. s.*	fʒ III

There are two ways of preparing the above. If compounded in the order in which it is written, the castor oil and the turpentine will separate. However, if the castor oil (1 ounce) is mixed with the stronger ammonia (1 ounce) by shaking well in a bottle, and the turpentine is then added little by little, no separation will occur. Care must be taken that the ammonia does not evaporate.

"In conclusion, I wish to state that the samples presented here do not only apply to these particular prescriptions. Very often pharmacists come across similar prescriptions and therefore it is advisable that these prescriptions be kept on file so that they may be used as guides."

EVALUATION OF TRAGACANTH AND TRAGACANTH MUCILAGES.*

BY ADLEY B. NICHOLS.[1]

During the revision of the National Formulary VI it became the writer's task to develop a formula for a jelly of ephedrine sulfate. Obviously, one of the first questions to be considered was how much tragacanth should be used. Using as controls several jellies which were on the market, a formula was developed for a preparation which seemed to closely simulate the general gel consistence of the available products. The tragacanth which was used in the experiments was labeled number one, which would have seemed to indicate that it would be of the first order.

VARIATION IN JELLY OF EPHEDRINE SULFATE.

When the formula calling for 2.7 per cent of tragacanth was published in the N. F. bulletins the response was indeed surprising. From one side came the request to "use more of the tragacanth." Another stated that the jelly "is about the same consistency as the '—' preparation," while from another source came the report that "the formula will not make a satisfactory product as it contains entirely too much tragacanth, making a very thick jelly." The latter individual suggested the formula which now appears in the N. F. It contains one per cent of tragacanth which makes the above comments all the more interesting.

Strangely enough, one of the first calls the writer received after the appearance of the N. F. was one complaining that the Jelly of Ephedrine Sulfate gave a liquid preparation, and other reports of a similar nature followed. Needless to say the answer apparently was to be found in the type of tragacanth employed.

With this rather unique background, experiments were undertaken to develop a method whereby an ephedrine jelly of the proper consistence could be prepared from any given lot of tragacanth. The nature of the work has been such that it is not yet possible to state the exact detail of such a procedure for ephedrine jelly itself. However, some extremely interesting results are available and it appears that a most sensitive evaluation of tragacanth and tragacanth mucilages is possible.

FALLING SPHERE TEST METHOD.

With the desire to develop a method which would be within the scope of practicability for the retail pharmacist, various standard viscosimeters were eliminated, while the possibility of using a falling weight seemed to offer an opportunity for development. Fortunately, just as work along this line was started, a reference to the identical idea was found in the work of Middleton in the *Quarterly Journal of Pharmacy and Pharmacology*, Vol. 9, pages 493 and 506 (1936). It was also discovered that the work of Middleton on the evaluation of tragacanth and tragacanth mucilage had been included in the British Codex of 1934 and, the data thus found, materially aided this project in many instances.

Briefly, tragacanth is evaluated by first carefully preparing mucilages of different known concentrations and basic uniformity throughout. Under stand-

* Section on Practical Pharmacy and Dispensing, A. PH. A., New York meeting.

[1] From the Pharmacy Laboratory of the Philadelphia College of Pharmacy and Science.

ardized conditions steel balls are timed as they fall through the mucilages for given distances and the results are plotted to give a curve from which it appears that mucilages of any specifications may be prepared. Comparison of curves also indicates the relative values of specific tragacanths.

Until experience has been gained with whole tragacanth, and always with the powdered drug, it is necessary first to prepare and test one or two trial mucilages to determine the general or rough value of the gum. For gums which would fall in the official class, this would consist in preparing for instance, a 1:50 and a 1:80 dilution. By reference to the typical curves the results of the preliminary test would place the tragacanth in an approximate position of value. Then a series of seven or eight dilutions are carefully prepared each different from the next by five units, thus: 1:50, 1:55, 1:60, 1:70, 1:75 and 1:80. If whole tragacanth is being used it is desirable to grind it sufficiently to make the individual portions representative of the entire lot, otherwise considerable variation may be experienced. On this same basis, not less than five Gm. of tragacanth and not less than 300 cc. of water seems desirable for the preparation of any mucilage. Needless to say, the tragacanth should be weighed upon a good balance and the water should be carefully measured, using a graduated cylinder or it might even be weighed if necessary.

The mucilages are started late in the afternoon, placed in liter-bottles to allow for agitation, shaken intermittently until the gel begins to form, automatically suspending the particles, then allowed to stand over night and again shaken as necessary to produce a uniform mixture comparatively free from lumps. A standard No. 3 Coors Porcelain Gooch crucible is set up in a liter suction flask fitted with a Walter crucible holder and suction is applied to the flask. A Richards' filter pump (aspirator) serves admirably for this purpose. The mucilage may be poured or shaken carefully into the crucible, or a Bailey crucible holder may be placed on the top of the crucible and the bottle inverted over this. By the latter procedure the mucilage is drawn from the bottle by suction. Care must be observed to empty completely the bottle, particularly any small remaining clumps, and all material should be forced through the crucible. The mucilage is then transferred to a beaker. If the mucilage is thin it will pour readily, but if it is thick the remaining traces should be scraped out. It is again drawn through the crucible and the process repeated at least a third time and as many more as required to produce a mucilage free from lumps and stringiness. The flask is then stoppered and the air is withdrawn completely by means of the vacuum pump. Violent agitation of the mucilage in the flask will help to clear the preparation toward the end of the operation after the vacuum has been applied for about ten minutes. Elimination of air bubbles is essential to obtain accurate reading. A portion of the mucilage is now poured carefully into a 25 mm. × 200 mm. test-tube to within about one inch of the top. Pyrex test-tubes seem to be desirable as they are of uniform diameter while some others which are available are found to be less than 25 mm. wide. Narrower tubes might have a constricting action on the speed of the ball. The tube which has been graduated previously to 10 cm. from a point about three cm. from the bottom of the tube, is stoppered and placed in a water-bath at 25° C. and kept there for one hour. It is then removed and suspended in a perpendicular position (suspension in a 100-cc. graduated cylinder was found to be most convenient). The cork is removed and another one, centrally fitted with a piece of glass tubing about seven or eight cm. long and having a bore of 5 mm., is inserted in such a manner that the tubing dips into the mucilage about one cm. A small slit should be made in the side of the cork to allow for expulsion of air.

One of the steel balls[1] (1/8 inch diameter, 0.130 Gm. in weight) is dropped into the centralizing tube and eventually passes into the mucilage proper. It will be noted that specifications for this tube and directions for its use have been given previously. The tube obviously insures that the consecutive balls will follow the same course which we will see is essential. By having the

[1] The balls used in these experiments were purchased from the Atlas Ball Co., Phila., Pa. Being high-grade bearings they run uniform in size and weight.

tube dip into the mucilage sufficiently the ball is checked in its initial fall and enters the mucilage proper free from any attached air bubble. If the mucilage is thin and the tube does not dip into it to the proper degree the ball will often carry an air globule with it, the latter retarding the fall of the ball through the measured column of mucilage. By placing the 10-cm. graduation near the bottom of the test-tube, sufficient space is allowed above the upper graduation to give the ball an opportunity to develop normal momentum before its speed is timed. The number of seconds required by the ball to travel 10 cm. is recorded, after which four or five additional balls are likewise timed.

It will be observed from Table I that the first ball always travels slower than those which follow, there being a marked difference between the time for the first and the second balls, with less variation between the second and third and those which follow. This explains the need for the centralizing tube which must be maintained in the same position until the tests have been completed. The path of the first ball apparently orients the colloidal particles of tragacanth along the central axis, thus making it easier for subsequent balls to follow. If a test on a certain mucilage is to be remade it becomes necessary to pour mucilage into another clean tube and not attempt to repeat the test upon the original tube. It is not even possible to run tests on an original tube on successive days without noting the above-mentioned effects of the first run of tests. When the tests are completed, the tubes are stoppered and then inverted to recover the steel balls. When subsequent tests were made even a day later, in this same material and tube, it was found that the speed of the ball reversed itself and instead of approaching a lower limit it approached a higher one. This was probably due to the particles being turned "inside out" when the tube was inverted for the removal of the balls. When the time for two successive balls does not differ by more than one or two per cent, the average of these two is taken as the final reading for that particular mucilage. Thin mucilage will show a greater degree of uniformity with fewer balls than will thick mucilage. It has not seemed necessary to use a constant temperature bath during the actual tests although it is desirable to perform the tests in a room as near 25° C. as possible. With heavy mucilage which may require up to ten minutes per ball, the possibility of any marked change in the temperature should be considered.

PLOTTING THE RESULTS.

When the time of fall of each dilution is plotted upon ordinary graph paper the result is a curve which is gradual, beginning with the high dilutions (thin mucilages) but rises abruptly with low dilutions (thick mucilages). Such a curve is difficult to use in this instance but by plotting the dilutions of the mucilage against the logs of the seconds of time of travel, the result appears to be a straight line, with

TABLE I.

Dilution of Tragacanth No. 12, 1 in - - - -	55.	60.	65.	70.	75.	80.	85.	90.
Time of Travel in Seconds	758	394	195.0	94.0	71.0	35.0	20.4	18.0
	615	342	166.0	80.0	60.0	29.5	18.0	15.5
	608	321	156.4	77.0	56.6	28.0	17.0	14.7
	...	310	?	75.0	55.7	26.8	16.0	14.3
	...	302	?	72.3	54.1	27.0	15.7	14.0
	...	299	145.0	72.1	54.6	...	15.5	14.0
Final Seconds	**610**	**300**	**145.0**	**72.2**	**54.5**	**27.0**	**15.6**	**14.0**

Complete results of tests upon several dilutions of a specimen of tragacanth.

the lines of various specimens approximately parallel. The range of operation is much greater and the accuracy of further estimated readings becomes much greater also.

TABLE II.—TIME IN SECONDS FOR BALL TO TRAVEL 10 CM. TEMP. 25° C.

Dilutions of Mucilage.	No. 12.	No. 13.	No. 14.	No. 15.
45	...	...	...	768.0
50	...	...	...	225.0
55	610.0	370.0	...	83.8
60	300.0	197.0	390	73.6
65	145.0	100.0	196	27.2
70	72.0	53.0	128	17.6
75	54.5	31.0	85	6.5
80	27.0	21.0	51	...
85	15.5	11.5	42	...
90	14.0	...	19	...

Final results of tests upon several dilutions of various tragacanths.

Table I shows the complete figures for a set of seven dilutions of one variety of tragacanth which were run simultaneously. Table II shows the final results of similar sets for four varieties of tragacanth.

In Fig. 1 are found the graphs which result when the figures of Table II are plotted as directed. It will be observed that the curve is of the straight line order and undoubtedly closer results would have been obtained, for instance, by grinding the tragacanth to even greater fineness,

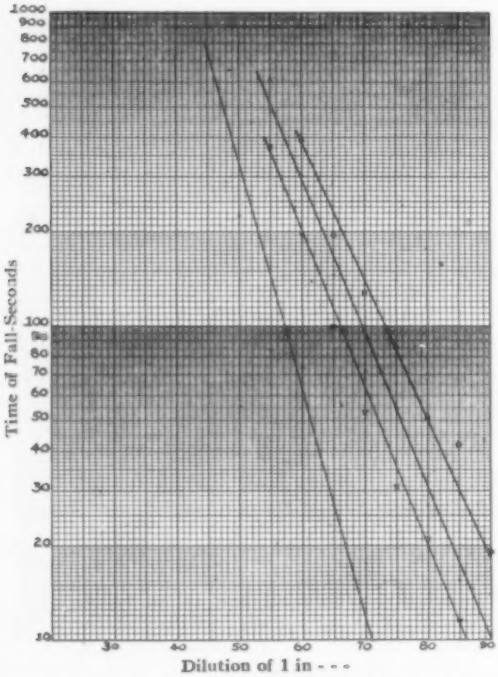

Fig. 1.—The curves from left to right are for tragacanths 15, 13, 12 and 14.

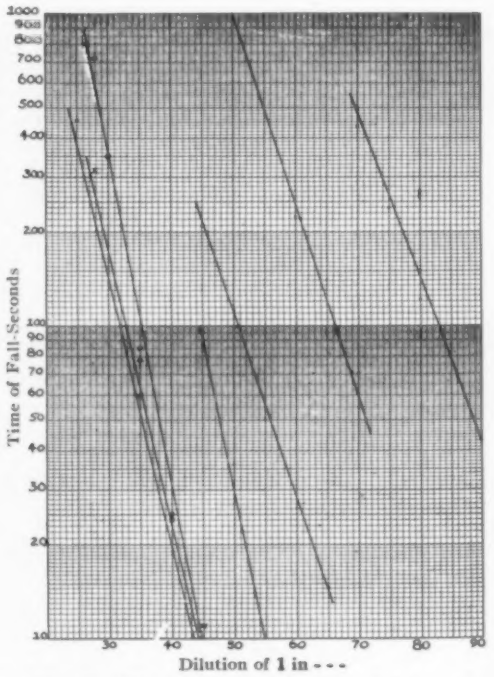

Fig. 2.—The curves from left to right are for tragacanths 2, 4, 11, 1, 8, 10 and 9.

the specimens in this case having been coarsely ground in a mortar without having made any attempt to specifically regulate the exact degree of fineness. From observations made throughout the work it is apparent that discrepancies occur when the whole pieces of tragacanth alone are

TABLE III.

Tragacanth Number.	Dilution 1 in - - - Rate of Travel in Seconds. 25.	28.	30.	35.	40.	45.	50.	55.	60.	65.	68.	69.	70.	75.	80.	81.	84.	85.	86.	90.
1						87.0	27	9												
2	−457			45.0	19/29° C.	8.8	36	9.2												
4		−316		59.5	24/26°	11.0														
8						209	112	50/26°	26	14.5										
9												492		150						
												432	239	95		47	87.0	69	43.0	
														92						
10							952		224	140/27°	90	70.5	55		122/26°					
													71							
													70/26.5							
11	−720	350	85		25	9.3														
12			78				−2010		232?	192		130	57.7	27.0	27		15.5		14.0	
									259?			107	54.5	29.5					16.4	
									343			89							18.0	
												72							19.0	
13						−2340	370		197			37	31.0	21.0			11.5		6.0	
									295	100		53		29.3						
14									330	193		119	85.0	46.0			42.0		27.3	
									780			128		51.0					19.0	
15						708	225	83.5	111.5	27.2		17.6								
							325		73.6			26.7	6.5							

Composite results of miscellaneous tests upon various specimens of tragacanth.

used. One portion may contain an exceptionally heavy piece which will produce a different mucilage than will the thin pieces; some tragacanths are made up of pieces of varying colors from white to yellow and each of these produces a different mucilage. Tests using larger quantities would obviate some of these differences also.

Figure 2 represents the composite results of tests, as also indicated in Table III, made at different times during the course of the experimental work. Some mucilages were prepared from whole tragacanths while other mucilages of the same specimen may have been prepared with the coarsely ground product. The laboratory temperature varied considerably on different days, and it is to be noted that the temperature at which a mucilage stands during the course of its preparation will cause a variation in the consistence of the mucilage. As an example, two mucilages of the same dilution were prepared, but one was made and stored at 25° C. while the other was held at 33° C. The former gave a reading of 63 seconds while the reading for the latter was found to be 88 seconds, which shows what a variation 7° will make. This factor may possibly need to be considered further. It will be observed that even in Fig. 2, composed as it is of a heterogeneous collection of data, the results still indicate curves of the straight line order.

TABLE IV.—IDENTITY OF TRAGACANTH SPECIMENS.

1. "Tragacanth A"—Whole—Wholesale Druggist No. 1.
2. "Powdered Tragacanth"—Manufacturing Pharmacist.
3. "Gum Tragacanth, No. 1 Flake"—Drug Importer No. 1.
4. "Tragacanth Gum, No. 1 Flake Powd."—Importer No. 1.
5. "Gum Tragacanth, No. 2 Flake"—Importer No. 1.
6. "Gum Tragacanth, No. 2 Flake Powd."—Importer No. 1.
7. "Gum Tragacanth, Aleppo Ribbon No. 4"—Importer No. 1.
8. "Gum Tragacanth, No. 4 Ribbon, Powd."—Importer No. 1.
9. "Gum Tragacanth, Ribbon, Extra Select"—Importer No. 1.
10. "Gum Tragacanth, Ribbon, Powd. Extra Select"—Importer No. 1.
11. "Powd. Tragacanth, No. 1."—Importer No. 1.
12. "Gum Tragacanth, Aleppo No. 1."—Jobber, Essential Oils, etc.
13. "Whole Tragacanth."—Drug Importer No. 1.
14. "Gum Tragacanth, Ribbon Aleppo No. 1—Whole U. S. P."—Drug Importer No. 1.
15. "Tragacanth A"—Whole—Wholesale Druggist No. 1.

TRAGACANTH EVALUATION.

An examination of the labels of the various tragacanths (Table IV) indicates that many of an inferior nature might be expected to be far more valuable than they actually are. The physical appearance of numbers 3, 5 and 7 would eliminate them from any such consideration for they obviously represent very poor grades of tragacanth. Knowing that 4, 6 and 8 are powders of these respective whole drugs would eliminate them at this time, but individually, of course, they look about alike in the powder form. Number 1 generally would be considered as satisfactory on its appearance and the source of number 2 would have acted as a voucher for it under normal conditions. Numbers 9 and 10 would be accepted without question, as would 11, 12, 13 and 14, although by physical comparison a difference in color might be noted as is the case in number 15, which contains many yellow pieces.

However, with the graphs of Figs. 1 and 2 available an entirely different story presents itself. It now would appear simple to interpret the relative value of each specimen of tragacanth in accordance with its placement upon the chart. One readily observes that numbers 2, 4 and 11 are poor products, and numbers 12, 13 and 14 are good varieties while number 9 actually would rank first.

A closer observation and study will give an actual numerical rating for each specimen based upon the dilution required for a certain number of seconds. If, for instance, 100 seconds is accepted as a standard, then number 2 tragacanth would be

required in a dilution of about 1 to 32 while number 8 would require a 1 to 51 dilution and number 9 would produce the same 100 second reading with a dilution of about 1 to 83. The actual ratings which might be given to these several specimens according to the falling sphere method appear in Table V.

TABLE V.

Tragacanth Number.	2.	4.	11.	1.	8.	15.	13.	10.	12.	14.	9.
Dilution 1 in - - - - for a 100 second reading	32	32½	35	45	51	56	65	66	69	73	83

Evaluation of Tragacanth Specimens.

U. S. P. TRAGACANTH.

Adoption by the U. S. P. of a method for tragacanth evaluation based upon this general procedure would seem wise in the light of the foregoing results. This would be in line with the British Codex which provides a time limit which a certain dilution of tragacanth must meet. It would appear from the above records that the U. S. P. might well expect a dilution of not less than 1 to 60 to produce a reading of 100 seconds. Such a test surely would advance the status of the U. S. P. monograph for tragacanth.

JELLY OF EPHEDRINE SULFATE.

Just as tragacanth itself might be judged and valued by a series of tests as described, so also it would seem quite possible to use these same results in the development of a uniform Jelly of Ephedrine Sulfate. Experiments along this line are now being conducted in the attempt to determine the "second" value for that tragacanth mucilage which seems to give a finished jelly of the proper consistence. Once such a record is established it should be simple, to again test an unknown tragacanth, plot the results and from the graph calculate the dilution which will give the desired mucilage, just as the dilutions in Table V would be expected to produce an approximate "second" value of 100.

TABLE VI.

Mucilage Number.	Reading in Seconds. 1st Day.	2nd Day.	4th Day.	5th Day.	13th Day.	35th Day.
1	56	64.5	75.6	76.5	104.0	136
2	28	31.0	34.6	35.2	48.6	68
3	...	16.2	18.5	18.8	25.5	37
4	140	...	203.0	...	...	400
5	...	70.5	83.0	...	111.0	...

Effect of age upon mucilage of tragacanth.

There are several additional factors which require consideration, however. Tragacanth mucilages become thicker upon aging as is indicated in Table VI. Heat, as we have noted, also increases the viscosity and both of these factors are being studied at present to determine the best possible solution to the problem of a uniform Jelly of Ephedrine Sulfate. Will it be practical to direct a given amount of heat to produce a maximum viscosity at once? Will it be practical to age the jelly for a given period of time? What will be the solution?

A further observation is that it would be desirable to strain the tragacanth mucilage at least through the Gooch crucible to assist in obtaining a smooth and

uniform jelly. Those who have some form of a colloid mill or homogenizer available will find that if the mucilage is processed by one of these units the resulting product will lose its characteristic granular or grainy appearance and will become perfectly smooth, adding materially to the appearance of the finished preparation.

CONCLUSIONS.

1. Jelly of Ephedrine Sulfate N. F. necessarily does not have the same viscosity when different specimens of tragacanth are used in preparing it.
2. Tragacanth U. S. P. varies to a marked degree in its mucilage qualifications.
3. A method is proposed whereby U. S. P. tragacanth would be required to pass a satisfactory mucilage test, based upon the time required for a steel ball to fall a given distance through a mucilage of definite concentration.
4. A Jelly of Ephedrine Sulfate of uniform viscosity may eventually be developed by using the falling ball method to determine the quantity of any given tragacanth to use in preparing the jelly.

MEDICAL ECONOMICS AND PHARMACY.*

BY R. T. LAKEY.[1]

In order that the best interests of the medical profession and of the public be served, all medical economics committees should be composed of carefully selected individuals appointed to represent each of the groups directly concerned in the costs of medical care. The nurse, dentist, clinical technician, social service worker and pharmacist are professionally related and interdependent. They all have a part in the proportionate distribution of the health dollar; therefore, a comprehensive consideration of health service economics, to be effective, must be inclusive rather than exclusive in character.

The medical profession is bound by a traditional code of ethics which prevents its members from undertaking for themselves and for their profession the dissemination of a type of propaganda which might help in correcting to a large extent professionally and socially dangerous trends.

The pharmacist is in a strategical position, because of his public contacts, to do a great deal of effective missionary work for the independent practice of medicine. That he has not done this in the past is partly the fault of the medical profession in not officially including him as a part of the professional family concerned with medical care. There is a sound psychological foundation for the belief that, had organized medicine given attention to its pharmaceutical needs, and had it exercised a certain amount of control relative to the development of educational standards and legislation affecting pharmaceutical practice, the drug store of to-day might be different. If he, the pharmacist, had been given proper recognition he might have developed professional pride and with it social consciousness to a greater extent. Without the advantages of such recognition, with its implied advice, guidance and coöperation, he has gone a long way in establishing for himself sub-

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* Section on Education and Legislation, A. PH. A., New York meeting, 1937.

[1] Dean, Wayne University, College of Pharmacy, Detroit, Mich.

stantial educational and practice standards, but he has been unable to control, except in pathetically few instances, the development of the drug store.

The American drug store is one of the products of a false conception of what constitutes true democracy. Until comparatively recent times we have been led to believe that individual investments of capital were sacred as long as they were legal. The broader concept of democracy, which limits the individual's prerogatives so that he may be assured of serving society properly and completely within his field of training, provides for the establishment of equitable and functional relationships of practice wherein maladjustments produced by economic stresses and strains have no place and wherein the public is better served by arbitrary control. Considering the drug store in this light, there is no logical reason for continuing a practice of uncontrolled investment in a business so vitally and so essentially concerned with public health and welfare as is the drug business. In a real democracy each unit of service, particularly health service, should be provided with limitations so that it will be unnecessary for it to expand its services to the point of destructive competition with other units in order to gain a livelihood for its devotees.

It is upon this vital point of professional maladjustments that the joint committees of organized medicine and pharmacy can meet with official sanction and support, on a basis of equality of professional recognition, of similarity of objectives and of unity of purposes, for mutual benefits harmonious with public welfare and social progress.

Every local branch of the AMERICAN PHARMACEUTICAL ASSOCIATION should see that it has official representation on all committees concerning themselves with the economics of health services.

THE RÔLE OF THE PHARMACIST IN CONNECTION WITH PUBLIC HEALTH WORK.*

BY B. E. HOLSENDORF.[1]

Modern public health work embraces many activities, draws from the general field of science as well as from medicine, sanitary engineering, chemistry, pharmacy and nursing, and as stated by Mustard, covers almost everything from constructing water supply systems to pasteurizing milk.

Its objective, as Dr. Mountin of the Public Health Service has so aptly expressed it, is to postpone death and to promote physical and mental well-being during the life span of the individual. In other words, public health work has for its purpose the prolongation of life and the prevention of suffering, particularly from diseases and conditions which are preventable or which can be controlled.

Knowledge of what diseases constitute public health problems and the factors which are responsible for and favor their propagation and spread is essential to the solution of these problems and to the attainment of the objective mentioned.

Fundamentally, the factors which have to be considered in this connection are:

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* Section on Practical Pharmacy and Dispensing, A. PH. A., New York meeting, 1937.

[1] Passed Assistant Pharmacist, United States Public Health Service.

(*a*) The causative agent
(*b*) The susceptible or non-immune person
(*c*) The means by which the infection is spread
(*d*) The measures of control.

Logically, therefore, the prevention of the propagation or spread of diseases that fall in this category hinges on the elimination or control of one or more of these factors.

A program for public health work must embrace the following fundamental activities which are essential to its success.

1. Collection of scientific data and information through surveys, inspections, investigations, laboratory findings, etc.
2. Outlining of plans and providing ways and means for effecting satisfactory control of the factors and conditions which are responsible for or favor the spread of such diseases.
3. Dissemination of pertinent information on public health problems to the special groups and units of the population which it is deemed desirable to reach.

In other words, information as to the cause of communicable diseases, the way in which they are spread and the measures which should be taken to prevent their further dissemination, and to control or cure them, should be imparted to the public so that the people may understand what is being done, and in order to secure coöperation and support.

What rôle can the pharmacist play in connection with the carrying out of such a program? What part or parts can he take in the prosecution of such work and how can he lend the most effective aid and coöperation?

The elimination or control of the causative agents and carriers and the correction of conditions which are responsible for or are favorable to the propagation and spread of disease involves the employment of many measures of a scientific, technical and practical nature.

In order to attain the desired public health objective it may be necessary to build water supply and sewerage systems, install sanitary privies, re-locate or rebuild wells to prevent pollution of the drinking water, eliminate or control mosquito, rat and fly breeding, prevent or protect milk and other food supplies from contamination with infected material. Many of these activities are usually so specialized that they do not come within the routine sphere of the daily activites of the average pharmacist. Control of some of the carriers, however, are problems which are very frequently brought to the attention of pharmacists, even though the purpose of control is not intended primarily as a public health measure, but rather to prevent personal annoyance and economic loss. However, when one stops to consider that the presence in a community of these potential carriers of disease constitutes a permanent menace to health, and the effect which their elimination or control has on the reduction or removal of such risks, it will be seen that the average pharmacist in the daily conduct of his business and the practice of his profession can and does assist in the promotion of such control.

Pharmacists can and do render effective aid and coöperation in that branch of public health work which relates to the protection of individuals from communicable diseases through immunization. In many communities they are the sole custodians and distributing agents of these valuable aids to disease prevention and control.

They should and do regard the keeping of a stock of active standard biological products and preserving them from deterioration as a sacred trust, for they realize that the time element is a most valuable factor in their administration and that delays are often fatal.

Valuable service of a public health nature is rendered when a pharmacist dispenses curative agents which have been prescribed to assist in the restoration to normal health of persons suffering from communicable diseases, thus eliminating them as carriers or foci of infection.

Another field of usefulness, and one which offers the widest range of opportunity is in the distribution or "dispensing," as it were, of authentic information on public health matters. I am using the term "dispensing information" advisedly, and in deference to the section under which this talk is given. Public health officials recognize that education of the public is one of the most important functions on their program, and that the best results are obtained when people are reached through personal contact.

The unique position which the pharmacist occupies in the average community, the confidence which is reposed in him by a great many of his fellow citizens, the almost daily contacts which he has with them, provide a most ideal medium for the dissemination of scientifically correct, practical and concrete information on matters relating to public health.

However, in order to "dispense" such information, the pharmacist should have more than a speaking acquaintance with the subjects connected with public health work, and be familiar with the programs which have been outlined and the objectives to be attained. It is noted with satisfaction that provision is being made for the teaching of many of these subjects in our colleges of pharmacy. The acquisition of this knowledge will not only benefit the pharmacist but will enable him to impart scientific information on matters related to public health to interested persons.

There are a number of communicable diseases that are health menaces and constitute community, sectional or regional public health problems. There are other diseases that are so widely spread over the entire country and each year exact such a heavy toll in lives and permanent disability that they have to be considered as national health problems.

The prevalence of venereal diseases presents such a problem, as well as the opportunity to combat its ravages and to prevent its further spread.

The Public Health Service acting as the national health agency, has outlined a nation-wide campaign for the control of venereal disease, which provides for examination of persons by competent physicians to insure the making of an early diagnosis, medical supervision of persons found to be infected, the administration of curative measures and its continuation until the infected person has completely recovered.

The present Surgeon General, Doctor Thomas Parran, who has had many years of experience in the work of venereal disease control, believes that pharmacists can render most effective service in the carrying out of this special public health activity, if they will:

1. Familiarize themselves with the various laws, ordinances and regulations bearing on this subject to the end that they may be in a position to give authoritative advice to persons who may apply for same.

2. Decline to treat persons suffering from venereal diseases but to refer them to reputable physicians and clinics for examination and treatment.

3. Restrict the dispensing of prophylactic and disease preventive agents and material to those which comply with approved and accepted standards.

Suggestions similar to these have been advocated by the Public Health Service for a number of years and are contained in the later editions of Remington's Practice of Pharmacy.

In the light of what has been said in connection with development of the subject of "The Rôle of the Pharmacist in Connection with Public Health Work," the question may very naturally be asked, "Will the average pharmacist assist in carrying out this specific program along the lines indicated?"

It is conceded that the forward-looking men connected with pharmacy, the men with visions, feel that pharmacy should take a more active part in public health work, and are willing to devote their time and talent to such service under one or more of the fundamental activities mentioned; research, control and curative measures, and dissemination of public health information.

Is it not fair to assume that a similar attitude will be maintained in respect to this special program which has been outlined for venereal disease control?

The carrying out of this special program, from the angle of the pharmacist's participation in it, is in harmony with the fundamental program outlined for general public health work, *i. e.*, the dissemination of public health information and advice and the dispensing of prescribed curative agents and approved protective and preventive agents. This is ethical pharmacy of a high order.

Assuming that there may be some financial loss involved in certain instances, it is believed that this loss will be more than compensated for by the gains in other ways which will be made, *viz.*: the recognition of the value of the aid which a pharmacist can render in the work of promoting public health and by his inclusion in the organized groups that are officially engaged in such work.

To sum up the situation, it would appear that there are three major lines of endeavor in public health work in which the pharmacist can participate:

1. Research and analytical work, especially that which pertains to biological products, narcotic drugs, curative and preventive agents and foods.

2. Distribution or dispensing of material required for use in the destruction or control of carriers of disease, or for the protection of the individual from infection, and the medicinal and other curative agents which may be necessary to restore to normal health those who are actually infected with communicable diseases.

3. Dissemination of information on matters relating to public health. Not the wholesale or promiscuous distribution of pamphlets or circulars to the general public, but specific and pertinent information given to persons who have need of same, because of the fact of the presence of infectious or communicable diseases in their homes or neighborhoods, and are interested in acquiring authoritative information on such subjects and are then in a psychological frame of mind to receive and make proper use of it.

In addition to Pasteur, whose research work and findings have aided so much in the solution of some problems connected with public health, many pharmacists and chemists have made valuable contributions to such work along one or another of the fundamental lines indicated.

The field for such service will broaden and the opportunity for engaging in such work through the organized agencies will increase in just the proportion that

the pharmacist prepares himself to take advantage of them and to discharge the duties therein involved.

What constructive public health work could be carried on and what beneficial results might be accomplished if this trained group of American pharmacists could be enrolled in the army of public health workers for service during the duration of this and all other future wars which may be waged on preventable communicable diseases; and, if all pharmacies could become outposts or health observation towers as well as auxiliary forts available for the use of all the forces engaged in the warfare on disease.

THE STATUS OF EXEMPT NARCOTICS UNDER THE UNIFORM STATE NARCOTIC ACT.*

BY ROBERT L. SWAIN.

The Uniform State Narcotic Act, the purpose of which is to supplement the activities of the Federal Bureau of Narcotics, has been passed in the following States:

Alabama	1935	Montana	1937
Arizona	1935	Nebraska	1935
Arkansas	1937	Nevada	1933
Colorado	1935	New Jersey	1933
Connecticut	1935	New Mexico	1935
Delaware	1935	New York	1933
Florida	1933	North Carolina	1935
Georgia	1935	Ohio	1935
Idaho	1937	Oklahoma	1935
Iowa	1937	Oregon	1935
Illinois	1935	Rhode Island	1934
Indiana	1935	South Carolina	1934
Kentucky	1934	South Dakota	1935
Louisiana	1934	Utah	1935
Maryland	1935	Virginia	1934
Minnesota	1937	West Virginia	1935
Mississippi	1936	Wisconsin	1936
		Wyoming	1937

The Uniform State Narcotic Act was the subject of several years' study by the Commissioners on Uniform State Laws, and as many as five separate drafts were made and subjected to extended study. The fifth draft was the one submitted to the American Bar Association at its meeting in Washington in 1932, and was officially approved by that body. The bill, as approved, was submitted to the legislatures of the various states in the following year.

As the name of the act indicates, its purpose was to make uniform the law in the various states with respect to controlling the sale and use of narcotic drugs. While it may be said that, in general, the state acts are uniform, they do differ in some important particulars. For instance, some state acts do not include Cannabis in the list of narcotic drugs. The penalty provision is different in some cases, and the agency charged with the enforcement of the State law differs in various states.

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* Section on Education and Legislation, A. PH. A., New York meeting, 1937.

It already appears that the definition of the term "Cannabis" is no longer adequate. In the uniform act, as originally adopted, Cannabis is defined as follows:

"Cannabis" includes the following substances under whatever names they may be designated; (*a*) The dried flowering or fruiting tops of the pistillate plant Cannabis Sativa L., from which the resin has not been extracted; (*b*) the resin extracted from such tops, and (*c*) every compound, manufacture, salt, derivative, mixture or preparation of such resin, or of such tops from which the resin has not been extracted.

At the instigation of the Federal Bureau of Narcotics, the Maryland Uniform State Narcotic Act was amended in 1937, so as to provide the following definition for the term "Cannabis:"

The term "Cannabis" as used in this Act shall include all parts of the plant Cannabis Sativa L., whether growing or not, the seeds thereof, the resin extracted from any part of such plant, and every compound, manufacture, salt, derivative, mixture or preparation of such plant, its seeds, or resin; but shall not include the non-resinous oil obtained from such seed, nor the mature stalks of such plant, nor any product or manufacture of such stalks, except the resin extracted therefrom, and any compound, manufacture, salt, derivative, mixture or preparation of such resin.

Even this definition differs from that in H. R. 6906, passed by Congress on July 28, 1937, which reads as follows:

The term "marihuana" means all parts of the plant Cannabis Sativa L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture or preparation of such plant, its seeds, or resin; but shall not include the mature stalks of such plant fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture or preparation of such mature stalks (except the resin extracted therefrom) fiber oil or cake, or the sterilized seed of such plant which is incapable of germination.

It was evidently the intention of the Uniform State Narcotic Act to give exempt narcotics a different status than is the case under the Federal Narcotic Act. It was the evident purpose of the Harrison Act to totally exclude exempt narcotics from its provisions. Section 6 of the federal act states "that the provisions of this act shall not be construed to apply to the manufacture, sale, distribution, giving away, dispensing or possession of preparations and remedies which contain narcotic drugs not in excess of the exempt proportions."

Of course, the federal act seeks to exert some semblance of regulation and control over exempt preparations, because it is specifically provided in the act itself "that such remedies and preparations are manufactured, sold, distributed, given away, dispensed or possessed as medicines, and not for the purpose of evading the intentions and provisions" of the act. However, in order to maintain the revenue aspect of the law, all persons dealing in the so-called exempt preparations must, under the federal act, be registered in Class 5, and pay a special tax of $1.00 per year. Under the federal act, there has been no limitation upon those who may register in Class 5. As a result, grocers, general dealers and other types of outlets have qualified under the federal law, and thus may lawfully sell exempt preparations. This has precipitated a rather odd situation, because, while there is no limit upon the type and kind of individuals who may deal in exempt narcotics, all of these persons are held to compliance with that provision of the federal act which limits the sale and distribution of narcotic drugs to legitimate medical needs.

Obviously, there is a conflict between the purposes of the Federal Narcotic Act

on the one hand and the liberality of the tax provision on the other. Certainly, if the purpose of the federal law is to confine the sale and distribution of exempt narcotics to legitimate medical needs, then it is most illogical to permit their sale and distribution by persons having not the slightest conception of what their legitimate medical needs might be.

It would appear that the Harrison Narcotic Act is in need of amendment, limiting the sale and distribution of exempt narcotics to those who may deal in narcotics generally. It is interesting to note that the Uniform State Narcotic Act passed in Iowa in 1937 meets this situation, as in a sub-section of Section 8, dealing with exempt preparations, it is specifically provided that

"nothing in this section shall be construed to permit any person to prescribe, administer, compound, dispense or sell any of the preparations included herein, except those persons duly qualified under this act to engage in the distribution of narcotics."

Further evidence that the provisions of the federal act with respect to exempt narcotics is unwise is shown by the recent act passed in California, under which the sales of all preparations containing morphine or opium in any quantity are restricted to physicians' prescriptions.

Obviously, the Commissioners on Uniform State Laws departed from the philosophy of the federal act because in Section 8 of the uniform act, dealing with the exempt preparations, it is expressly stated that "except as otherwise in this act specifically provided, this act shall not apply to the following cases: prescribing, administering, dispensing or selling *at retail*" of any medicinal preparation containing narcotic drugs not in excess of the exempt proportions. Inasmuch as there is no reference to exempt narcotics in any other section of the Uniform State Narcotic Act, it must be inferred that the Commissioners on Uniform State Laws did not mean to recognize exempt preparations except at point of retail sale. In other words, all of the provisions of the Uniform State Narcotic Act apply to exempt narcotics to the same extent and to the same degree as they apply to other narcotics.

This is further evidenced by the definition of "official written order" as it appears in the Uniform Narcotic Act. In Section 1, Sub-section 15, official written orders are defined as follows:

"Official written order" means an order written on a form provided for that purpose by the United States Commissioner of Narcotics, under any laws of the United States making provision therefor, if such order forms are authorized and required by Federal law, and if no such order form is provided, then on an official form provided for that purpose by the (Enforcing Department or Board).

Inasmuch as the federal law does provide for written order forms for the purchase of opium or cocoa leaves or any compound, manufacture, salt, derivative or preparation thereof, the only possible use for the State form, authorized by the Uniform Narcotic Act, would be for the purchase of Cannabis and its preparations and the so-called exempt narcotics. There can be no escape from the conclusion that it was the purpose of the Commissioners on Uniform State Laws, through the instrumentality of the Uniform State Narcotic Act, to surround Cannabis and its preparations and exempt narcotics with all the rigor of control and regulation with which narcotics in general are surrounded. This being done, it was considered sufficient liberality, in the light of the purpose and philosophy of the Uniform State Narcotic

Act, to permit Cannabis and its preparations and exempt narcotics to be sold at retail without the use of prescriptions or official written order forms.

It will be observed that the Uniform State Narcotic Act departs from the federal law by providing that official written order forms may be supplied:

(*a*) To a manufacturer, wholesaler, pharmacist or pharmacy owner.

(*b*) To a physician, dentist or veterinarian.

(*c*) To a person in charge of a hospital, but only for use by or in that hospital; provided, the official written order is signed by a physician, dentist, veterinarian or pharmacist connected with such hospital.

(*d*) To a person in charge of a laboratory, but only for use in that laboratory for scientific and medicinal purposes.

The effect of these limitations is to restrict the sale and distribution of Cannabis and its preparations and exempt narcotics to the foregoing persons and concerns, thus confining them to professionally trained hands.

Sometime ago I made a canvass of the situation in all of the states in which the Uniform State Narcotic Act had been passed, and found that in practically none of them was any enforcement activity being carried on. This is all the more surprising, because, as I have tried to point out, the Uniform State Narcotic Act includes Cannabis and its preparations and exempt narcotics, within the group of narcotics in general, with the single exception of the point at retail sale.

Some interesting questions immediately arise, once we understand the philosophy and purpose of the Uniform State Narcotic Acts, and we then begin to apprehend just why provision is made for the issuance of state official written order forms. For instance, how may a pharmacist, under the Uniform State Narcotic Act, obtain exempt narcotics for retail sale? The answer obviously is by means of the state official written order forms, for which the law provides. No sales at wholesale may be made of exempt narcotics except in pursuance of official written order forms. Inasmuch as the Federal official written order form may not be used for the purchase of Cannabis and its preparations and exempt narcotics, it then follows that the only order form which can be used is that provided for by the State enforcing agency. This is a matter of utmost importance, because it necessarily follows that in every state where the Uniform State Narcotic Act is in effect, and which has failed to provide the necessary state written order forms, all sales at wholesale have been in violation of the state act. This view is also held by the Federal Bureau of Narcotics, so I have been advised. This in itself is no small matter, when it is remembered that the Uniform State Narcotic Act provides penalties of great severity in cases of violations.

So far as I know, the only state which has made an attempt to deal with the situation is Maryland. In 1937, amendments were adopted to the Uniform State Narcotic Act in that state, under which authority the Maryland State Department of Health has provided official written order forms for the purchase of Cannabis and its preparations and exempt narcotics. The amendments themselves were instigated and sponsored by the federal government. Representatives of the federal government appeared before the State Department of Health urging this legislation, and they also appeared before committees of the Maryland legislature, to which the bill was assigned. The amendments became effective on June 1, 1937.

Unquestionably, there have been serious abuses of exempt narcotics. The

federal government has been aware of this situation, and it is for this reason, I believe, that it is showing a greater interest in a means of making the state laws more effective. The Uniform State Narcotic Act, when its provisions are brought fully into play, would seem to afford all necessary machinery for dealing with the situation so far as the states are concerned.

I have discussed the matter in this paper, though somewhat briefly, so that the attention of the state agencies themselves might be focused on the problem, as well as upon the responsibility placed on them by the specific terms of the Uniform State Narcotic Act itself.

LAW, ECONOMICS AND BUSINESS IN BUYING A DRUG STORE.*

BY JOSEPH H. GOODNESS.[1]

If we recognize that drug stores are purchased for economic reasons of income and profit rather than for the establishment of systematic charities, then we can accept the idea that no going drug business should be bought until a thorough investigation, economic, legal and business, is made, and that the income, the profit and economic security we desire are reasonably sure to appear. Before we venture into the discussion of what this investigation should be like, we must remember that there is no absolute guaranty, even after the most thorough investigation, of always gaining this economic goal.

An earnest investigation, however, will so materially decrease failure, that one who cannot afford to lose his investment must, in fairness to himself and family, investigate. Too many humans plunge into new ventures with hopes high and out of reason. Reality soon reduces such hopeful innocents to failure, all neatly classified under such technical headings as "Insufficient capital," "Inexperience," "Poor business location," "Poor management," "Competition" and a host of others.

A thorough investigation of a drug store consists of three parts: an economic investigation of the chances of future success, a business investigation of the enterprise to determine its worth, and a legal investigation to assure the buyer of limited liability and complete passage of ownership to him.

THE ECONOMIC INVESTIGATION.

The economic security and success we seek requires that we first examine the facts that may affect the future of the business. This investigation rests upon the principles and laws of economics, and consists of predicting, as best we can, the future size and nature of the *demand* for the goods and services of the store, the *monopolistic advantages* of the business, and the *competition*, both present and future, that the business must or may meet.

To know that the average store needs about 2100 of population to support it is not enough. A study of demand for the goods and the services of the store must be more searching. It begins with the present. What do the annual sales of the

* Section on Commercial Interests, A. PH. A., New York meeting, 1937.

[1] Assistant Professor of Economics and Business Administration, Massachusetts College of Pharmacy.

store amount to? Is the stock complete? If both answers are satisfactory we can assume that the business is running at top speed, and the future demand will, at best, be the same as at present. On the other hand if the sales amount is smaller than average for a store of its size, or the stock is incomplete, then we must look for the failures in services rendered. We have often heard it said that success depends upon services rendered, but have seldom, if ever, seen a listing of what may be considered the basic principles of service. Briefly, I believe them to be: *First*, giving customers what they want, and *second*, making customers feel important. It must be remembered that what a customer wants is not to be limited to the product he requests. His want, or rather wants, when he asks for four ounces of syrup of hydriodic acid, include a want of a clean container, a clean label, an air of confidence in the pharmacist, cleanliness of the store and clerks, sufficient bright lighting and innumerable other things. In some cases he may even want what he does not know he wants. So, a store that truly serves, sells with its syrup of HI the unconscious forces of confidence, exclusiveness, popularity (advertising), dignity, cleanliness, politeness, proximity, air conditioning, neat wrapping, ramps rather than stairs, delivery service, the aid of clerks who talk foreign languages, bright lights and other special services. If the store under question misses these qualities or some of them, then the chance of increasing the demand of the store's future services is excellent, providing that competitors are not already supplying the community with them. If competitors are aggressive, the best than can be expected, statistically speaking, is an increase of demand by half the difference between the sales of the two stores. For, by the laws of chance, business tends to divide itself equally among competitors rendering equal services.

Demand should be viewed from another angle, namely, that of the continuation of its existence. Neighborhoods change, traffic is rerouted, industries fail, parking is forbidden, changes in zoning laws bring new competitors, and each brings with it a failure of demand that formerly supported the store. While we cannot know the future, we must know the *present* facts that may affect the future.

Making customers feel important, the second factor that builds demand, is so foreign to economics that it is not discussed here.

The future economic success of the store was also said to depend on the monopolistic advantages it possessed. To-day, because of the ever-increasing number of drug stores, good roads, cheap transportation, mail order houses, the chance of monopoly through location and absence of competition is almost a theory. But the drug store may have a different kind of a monopoly. It may have own-label products, those that it sells under its own trade-mark or trade name. The demand this creates is truly monopolistic, and assures the continuation of business even if it does not always assure an extra profit. A less important type of monopoly exists in the sole agency for particularly branded goods of a manufacturer. While this was exceedingly valuable in the past, its worth has decreased considerably because of the ever-increasing number of lines of branded goods that are available for such arrangements with retailers.

The final step of economic investigation has to do with competition. While the druggist may recognize but one type of competition—the competition of the other druggist—there are really three types that he must consider. A mere mention of each should suffice. There is, *first*, the competition created by every other

merchant who wishes to sell his products or services. (The income of the average man is limited. If he buys one luxury, with his small excess of cash, he must forego all others until another surplus appears.) This type of competition has grown particularly vexing to the druggist through the activities of instalment sellers and the race tracks. The second type is that created by other vendors of drugs or items that a druggist sells. And the third type, that which exists upon the shelves of the drug store—the competition of one product against all others on his shelves that are used for the same purpose. The pell-mell growth of new remedies and proprietaries will soon be the major problem of the retail pharmacist if it is not that already.

THE BUSINESS INVESTIGATION.

Having estimated the demand, monopolistic advantages and the competition, we then investigate the store from the business angle. A vendor of a going business has tangible and intangible assets to sell, minus the liabilities. Or, to be more specific, he sells the merchandise, fixtures, accounts receivable, the lease, and good-will, and from this makes deductions for unpaid debts, and outstanding legal and contractual obligations.

Our investigation, then, is outlined. We must see that assets are as valuable as they are claimed to be, and that liabilities do not exceed those enumerated in number and amount.

The merchandise inventory should be examined for its age, valuation, ownership and quantity. There can be no better way of acquiring information on all these points than by taking a physical inventory—actually handling every piece of goods present. Old goods should be discarded as of no value to the buyer, and the value of salable goods should be given its cost or market value, whichever is lowest. As to ownership, there is, of course, no way that consignment can be identified by examination. The question is then for legal investigation. As to amount of merchandise, it is a known truth that the average drug store is overstocked. Whether the store you are examining is over- or understocked can be determined by a handy formula as follows:

Two-Thirds of the Annual Sales Divided by Inventory.—As you may recognize, the formula determines turnovers in the store. The sales figure is reduced here by one-third of its amount so that it will represent the cost of the goods sold. If the answer to this equation is *less than 3* (turnovers), this shows a tendency for the store to *overstock*. This decision is natural, since the average drug store should be doing between three and four turnovers a year. If the answer is *greater than 5* (turnovers), then there is a tendency toward *understocking*. In buying a drug store understocking is the lesser evil, for while it may have kept some customers away from the store because of the "We're just out, but will have it to-morrow" explanation, the lost customers can usually be attracted again by a change in policy. Overstocking, on the other hand, produces the possibility of overinvesting if not discovered by the buyer. When overstocking is discovered in the investigation, the price offered for the business should not exceed that paid for a properly stocked store. One should not undertake the burdens of former poor management.

The fixtures of the store should be examined as to condition, book value and arrangement. Of these points, perhaps only the valuation needs any comment. Unless the business has been depreciating the value of the fixtures regularly they

will be listed at the original value, a value which cannot be recognized. The other point on value of fixtures is that, even if new, they should not exceed in value from 10% to 15% of the average annual sales. This figure is determined by estimating the life of fixtures to be 10 (or 15) years and then allowing the usual one per cent of sales per year for depreciation. It may be added that "forced obsolescence" which results in making even fairly new fixtures "old fashioned" because of changes in style (such as modernism) makes it advisable to restrict the value of new fixtures to 10 rather than 15 per cent of average annual sales. This formula should be modified to fit the conditions. If there is only one year of service left in the fixtures, they should not be valued over one per cent of sales. If two years, two per cent, etc.

The accounts receivable should not be purchased if this can be arranged. Customers of the old management very often feel a sense of resentment in having to pay new owners. If the accounts are purchased, they should be purchased at very much reduced valuations. As a handy rule, accounts unpaid under one year are grouped and valued at 50%, and accounts between one and two years, 25%, and no value for those over two years old. This formula may be of little value if the business has a disproportionate quantity of accounts of long standing or if the accounts were created during a short period of time. The law allows actions to collect debts of this nature for as long a time as six years after they are due, but legal and business rights are not identical. If the original owner of the accounts could not collect them, feel sure that the new owner won't, except at such expense and trouble as to make the entire undertaking not worth while.

The lease should be examined next, and there should be a lease present unless the pharmacist is also the owner of the building. To plan on the purchase of a drug store that is operating without a lease of the premises should be undertaken only if the landlord has agreed *in writing* that a favorable lease (with the terms specified) will be given the new owner.

The absence of a lease gives warning to two important points, *first*, the possibility of terminating the stay of the new tenant without more than a trivial notice, and *second*, the slight or non-existence of value of the good-will of the business.

If there is a lease, the buyer should inspect it closely for the following: *First*, the lease should be transferable. There should be no terms forbidding assignment, for an assignment is valueless and generally voids the lease if a transfer is attempted when forbidden. *Second*, liabilities as rent, repairs, rebuilding, etc., of the tenant should cease if the premises are made unsuitable because of fire or other causes arising through no fault of the tenant. There are of course many other points to look for as, for example, renewal rights, but the above two have caused the greatest losses to unobserving retailers.

Good-will is the last, and perhaps the asset most difficult to investigate and evaluate. Our first problem is to determine whether it is present or not, then, if present, our second problem is to find out the maximum price we can afford to pay for it.

Realizing that money can earn up to six per cent a year in first mortgages and other safe investments without unreasonable risk, we can come to the conclusion that any drug store yielding less than six per cent net profit on the invested amount has no good-will. Net profits over six per cent on investment are evidences of the asset.

The courts have defined good-will as "the expectation of continued patronage" which to the business man means "the expectation of continued net profits." The value of this expectation is dependent upon the length of time it continues. If net profits are reasonably expected to continue for five years, then the seller may be justified in asking for part of this profit as the price of good-will. Just how much he can ask, depends upon a multitude of facts. As has been mentioned, the absence of a lease cuts the assurance of the continuation of profit to nothing, a short-time lease to a very small value, etc. All the economic factors of the store's future affect the value: as changing neighborhoods, the appearance of competition, the non-transferability of an exclusive agency, all destroy part or all of good-will.

Each investigation is a case unto itself. This willingness to surrender part of the net profits, coupled with the test of the existence or non-existence of good-will, has suggested to me a formula for checking the value of the asset. I say "checking the value" rather than "determining" it, because the formula can be used only after a price has been asked. It follows:

The average net profit *minus* 6% of the investment price *multiplied by* the number of years that net profit will be surrendered to the seller.

To explain the formula:

The buyer says, "I'll give up three years of net profits (because I'm reasonably sure of getting six or more years of like profits), but since my investment deserves six per cent income from any venture, I'll subtract that amount from each year's net profit before I surrender it." The reasoning here is without fault. In an example, using round figures, the process of applying the formula would be somewhat as follows: The seller having $6000 of assets in excess of liabilities, and making an average net profit of $2300 a year, asks $14,500 for the business. The buyer, after an investigation of the lease, economic demand, competition, etc., believes that the business can continue to produce the average net profit now being earned for six years more (the duration of the unexpired lease). The buyer is therefore willing to surrender three years' net profit after the subtraction of six per cent on investment from each year's net profit. His mathematics follows:

Three (years) *times* the difference between the average net profit and the six per cent on investment or

3 (2300 minus 870)
3 (1430) or $4290 (The value of the good-will to the buyer.)

To this good-will price he adds the value of the other assets of $6000, making the value of the business to him $11,720. His maximum price would therefore be about $12,000.[1]

To conclude the business investigation comments, the buyer should avoid assuming, if possible, the unpaid debts of the business. If they are assumed, they should be specifically listed; and a written statement should explain that all unlisted debts are not to be assumed. This exclusion can save many headaches for a new owner.

THE LEGAL INVESTIGATION.

In the legal investigation of the sales transaction and the going business, the buyer, with the aid of a lawyer, should examine the lease for the terms already mentioned. He should have all agreements pertaining to land and future leases in writing, for without writings such contracts cannot usually be recognized by the courts. (Statute of frauds.) Agreements and contracts involving sizable sums, or

[1] The mathematics is incorrect in that the six per cent was calculated on the high asked price of $14,500, and the offered price is lower, $12,000. But since the method is only for approximation, the error is immaterial.

acts that cannot be completed by the parties within a year of the making of the contracts, should also be in writing for the same reason. But the most important precaution that a buyer must take is to follow to the letter the bulk sales law that exists in most states. Briefly, this law requires that when a business is sold in other than the usual course of trade (item after item to customers over the counter), the creditors of the seller must be notified of the sale a certain time before the sale is consummated. Unless this is done by the buyer, seller, or both, as the law requires in the particular case, the unnotified creditors can consider the sale of the drug store as void, which in non-technical language means, even if the new owner has paid cash for all the goods, the creditors of the old owner not receiving legal notice of the sale can lay claims to the goods of the store *as though they were still owned by the old owner*.

Finally, the buyer should make sure that he is dealing with parties having complete authority to sell. This is particularly necessary when purchasing from corporations, partners, estates or court officers.

These, then, are matters that should be of heaviest concern to the investor in a drug business. Many minor matters, some too obvious, others too particular for discussion here, must also engage his attention.

THE INTERNATIONAL PHARMACOPŒIA OF 1885.*

BY EDWARD H. NILES.[1]

When the abbreviation P. I. appeared for the first time in the United States Pharmacopœia, IX—1916, it made American pharmacists definitely conscious of the attempt to establish world standards for many potent drugs and preparations. The abbreviation stood for Protocol Internationale, and its history can be briefly given.

In September 1902, there was held in the City of Brussels an important meeting, called The International Conference for the Unification of Potent Remedies. This conference formulated certain regulations for the strength of more than forty drugs and preparations. The delegates returned to their respective countries to urge that the various nations include in their pharmacopœias these proposed regulations. In 1906, representatives from nineteen countries, including the United States, met again in Brussels and formally signed the agreements proposed in 1902.

The above action ended a forty-year struggle to provide an international Pharmacopœia. But it is interesting and may be a surprise to some to know that at one time a complete International Pharmacopœia was prepared by an authorized commission, and a copy wholly in Latin was submitted to an international congress for ratification.

The advantages of an international pharmacopœia were long recognized, but the matter was brought to formal notice at the first meeting of the International Pharmaceutical Congress, held at Brunswick in 1865. While it was agreed that a Universal Pharmacopœia would be a good thing, no steps were taken to carry out the project.

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* Read before Section on Historical Pharmacy, A. PH. A., New York meeting, 1937.

[1] Dean, Indianapolis College of Pharmacy.

At Paris, in 1869, the Congress had a definite proposition in regard to the matter, and the Paris Pharmaceutical Association was given charge of the project. Two years later, at the Vienna meeting of the Congress, a wish was expressed for the speedy completion of the work.

At St. Petersburg, in 1874, the Paris Society submitted the manuscript of a pharmacopœia. This was carefully compiled, and showed evidence of great skill and unbounded zeal. While it conformed to the order of the Congress, it included too much and aimed too high. This awakened the delegates to the difficulties of the problem. The Paris Society was thanked for its efforts, and the Congress reconsidered the whole matter and promulgated preliminary plans for a more modest attempt.

At London, in 1881, a fresh start was made and a commission appointed to study the strength of preparations containing potent drugs, as found in the various pharmacopœias. At this time (and later) the greatest disagreement was in regard to the scope of an international pharmacopœia. Some felt that it should include only those few potent preparations in which a difference in strength in various countries might have a fatal result if a prescription were dispensed according to a different formula than the physician expected. Of course some others were of the opinion that a broader list of recognized medicinal agents would be more useful in such a pharmacopœia.

Before adjournment at London, a commission representing eighteen countries was named to study the potent drugs and preparations in the various pharmacopœias, and report to the President of the commission. Thirty-five members served on the commission, each country, except Greece, having two representatives. For the United States, John M. Maisch and Charles Rice participated. The president of the commission was Anton von Waldheim of Austria.

The sixth International Pharmaceutical Congress convened at Brussels, August 31, 1885, and adjourned September 5th. The meeting was held at the Palais des Academies and was truly elaborate. It was sponsored by the King and Princes, educational dignitaries, and government officials of Belgium. Americans at the opening meeting were Messrs. F. Stearns, Geo. J. Seabury and J. L. Creuse. The American flag was conspicuously displayed in the decorations of the grand stairway leading to the hall. When a number of honorary vice-presidents were chosen, Mr. Creuse was elected to represent the United States.

Consideration of the project of an International Pharmacopœia was the order of business for Saturday afternoon, September 5th. President von Waldheim, of the International Pharmacopœia Commission, gave his report. After a prefatory history, tracing the project from 1865 to 1881, he distributed copies of the proposed International Pharmacopœia. Notes and comments were given in both French and German, but the Pharmacopœia itself was entirely in Latin.

In selecting materials, the latest editions of the following seventeen pharmacopœias had been used; United States (sixth revision, 1882), Austria, Belgium, Denmark, Germany, Great Britain, Greece, Hungary, Italy, France, Netherlands, Norway, Portugal, Russia, Sweden, Spain and Switzerland. It is curious that two of the thirty-five members of the commission were from Ireland, but no Pharmacopœia from Ireland was considered.

As associate officers, von Waldheim had two vice-presidents and the secretary

of the commission; these were from France, Russia and Austria, respectively. In spite of language difficulties in the seventeen pharmacopœias, the president had prepared and sent to all members of his commission the draft of a proposed pharmacopœia, containing 232 articles. Of these, 188 were generally approved and 44 were struck out. In addition, the various members made their own selections until a total of nearly 500 articles was being considered. Finally, after much voting, the majority of the Commission agreed on a scheme giving a total of 293 substances and preparations.

Of these, 181 were printed in large type as being of special importance, and 112 were in smaller type. With each article was given information as to the pharmacopœias in which the article was official, and the votes for and against each article were also recorded. One of the most difficult tasks was to obtain a uniform and satisfactory Latin nomenclature. When we consider that the U. S. P. Revision Committee still changes Latin titles for some articles with each new issue, we are not surprised at the difficulty experienced in 1885.

The International Pharmacopœia gave for crude drugs the botanical and zoölogical names, habitat, part used and sometimes the time of collection and method of preservation. For preparations there were given clearly defined manufacturing processes. For chemicals there were given the physical characteristics and constants, and a limit of impurity.

It is impossible in this short paper to give much detailed information in regard to the articles included in this Latin Pharmacopœia. Of the 181 "important articles," about half are preparations. These are considered important because they occur in the majority of the pharmacopœias, are widely known and prescribed, and are more or less potent remedies.

In the "important" list are 56 chemicals and 30 crude drugs. The chemicals are both inorganic and organic, and include nine alkaloids or their salts.

Of the 112 "less important" articles, between seventy and eighty are preparations and the rest are drugs and chemicals. The larger portion of the less important list was not desired by a majority of the commission, but was included in deference to the wishes of a few. In this list were assumed to be those remedies which were of local importance only, or of obscure potency. However, there were included among the unimportant: Fluidextract of Ipecac, Tincture of Squill and Solution of Arsenous Acid, all of which are in the U. S. P. XI.

Of all the articles in the International Pharmacopœia, only about 50 were in every one of the seventeen national pharmacopœias examined by the commission. It seems rather surprising that such items as carbolic acid, morphine or its salts, spirit of nitrous ether, or chloroform were not in some pharmacopœias.

With a perspective of more than fifty years, we can view the voting on many items with interest, amusement and tolerance. An American member of the commission voted against having chloroform, calomel, sweet spirit of nitre, iodine, solution of lead subacetate or ether in the International Pharmacopœia. Apparently the Spanish members of the Commission were in an unyielding state of mind. Only about twenty-five articles received their approval; in many instances they cast the only negative votes, even against such items as Dover's Powder. Incidentally, two Norwegians cast the only votes against including Digitalis.

It seems like an anti-climax to have to state that this International Pharmaco-

pœia was not formally ratified by the sixth International Pharmaceutical Congress, nor at any later meeting. Nevertheless, a study of this document gives the most complete knowledge of any single source on the state of pharmacy and the medicines used throughout the world fifty years ago.

The writer believes that every teacher of pharmacy and pharmaceutical history should bring this topic to the attention of his students. Teachers of Pharmaceutical Latin may find many valuable exercises by using extracts from this complete Latin work. As reference for those interested, the *Chemist and Druggist* for 1885 gives a good account of the Brussels Congress and prints the Latin pharmacopœia complete. The *Druggists Circular* for 1885 describes the meeting of the Congress and gives an English translation of the International Pharmacopœia.

MEANING——?*

BY WILBUR L. SCOVILLE.

In writing or speaking it is easier to mean what we say than to say what we mean. As Wilson Follett puts it "the use of a wrong word most often denotes a broken link in one's acquired information" and "its meaning is that which our hearers supply for themselves."

A school boy is credited with defining a synonym as "the word you use when you don't know how to spell the word you should use." In many cases it might be defined as the word we use when we neglect to discriminate as to its meaning.

In legal matters the choice of words is highly important and legal documents are filled with seemingly superfluous synonymous phrases which are used to forestall technical or ambiguous interpretations.

Teachers who mark examination papers are painfully aware of the need to interpret, kindly it is hoped, phrases by the writers who may or may not mean what they say but do not say what they mean. Such faults are not confined to students. Are any of us wholly guiltless? How often are we saved from explanations by our comprehending audiences who correctly interpret our ambiguous phrases, particularly in scientific discussions? We may think that we have stated a subject clearly but our hearers may have understood because they are sufficiently familiar with the subject to grasp our meaning in spite of faulty statements.

Herein is the difficulty of writing popular articles on technical and scientific subjects. We need for this to be careful not only to mean just what we say but to say it in words which the reader will understand. The wise speaker or writer does not assume too much technical knowledge on the part of his audience.

Even such meticulous works as the Pharmacopœia and the National Formulary may slip in some of their phrases.

For instance, both books describe certain and several acids as having "an acid taste" or "an acidulous taste." To the chemist, who knows that many acids are sour in taste, in moderate dilutions, the meaning is plain. But not all acids are sour in taste. Barbituric and picric acids are bitter; benzoic acid is pungent and biting; boric acid is not sour; salicylic acid is first sweetish, then acrid; tannic acid

* Section on Education and Legislation, A. PH. A., New York meeting, 1937.

is astringent; oleic and stearic acids are bland; so in this group the term "acid taste" is without meaning.

Furthermore the strength of solution may make a difference in taste. Professor Kahlenberg found that hydrochloric, nitric, sulfuric and acetic acids in high dilutions—($N/400$ solutions) are astringent, while in stronger solutions ($N/200$ and stronger) they are sour.

So when an acid is described as having an acid taste it means what it says but doesn't say what it means.

The newer conception of acidity and alkalinity as expressed by hydrogen-ion concentration has brought some new phrases into use, and until the significance of these has become more settled some confusion in their use may be expected.

The logarithmic expression p_H 5.0 means a definite and understandable degree of acidity; likewise the expression p_H 8.0 means a definite degree of alkalinity. In themselves the expressions have definite meanings. But the expressions are mathematical and when they are qualified there is danger of confusion.

As an instance, under AQUA DESTILLATA is given a test or limitation of acidity, and the test is stated as "indication a p_H of not less than 5.8." To what do the words "not less than" refer? Do they refer to the degree of acidity? or to the mathematical expression?

If we regard them as referring to the amount of acid which should be present, then they mean that there should be not *less* acid present than is represented by a p_H of 5.8. Under this interpretation the water may contain more acid but not less. On the other hand, if the words "not less than" refer to the mathematical expression 5.8, then, since acidity increases with a decrease of p_H numbers, they mean that there must not be *more* than the amount of acid present which is represented by a p_H of 5.8. So less is more or more is less, according to how the phrase is interpreted.

In this case the test itself shows which is intended, but the phrase requires a chemist to properly interpret it.

To a layman the expression is ambiguous, a case of meaning what we say but not saying what we mean.

We cannot always be meticulous in our conversations and it may not be desirable at all times in our writings. I live in "a glass house" in this regard and have no right to be critical of others.

I have noted that errors are frequently long-lived, unless somebody labels them as such, then they die. I hope that I have said what I mean.

Edward Kremers speaking on "State Pharmaceutical History" before the New York meeting of the Section on Historical Pharmacy said:

"Unfortunately, not a few enthusiasts are of the opinion that they can write history without making adequate preliminary studies. In the *Badger Pharmacist* we have an illustration of how one student of the history of our pharmaceutical past has endeavored and is still endeavoring to bring together material for the future historian." No paper was presented for publication, but the speaker acquainted the Section with his preliminary studies so far as they are laid down in the *Badger Pharmacist*, copies of which were shown to the members with brief comments on each.

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

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ON MAY SIXTH of this year a conference on professional education was held in the city of Washington under the direction of the American Council on Education. This conference was attended by representatives of pharmacy, medicine, dentistry, law and engineering. The subjects under discussion were those things in education which the professions may have in common. At the moment the question which was uppermost was the question of cultural subjects. One member of the committee representing pharmacy was the Editor of the *American Journal of Pharmaceutical Education*. He was asked by a representative of the New York Department of Education why pharmaceutical educators insist on placing so much English or mother tongue in the pharmaceutical curriculum. The reply was that the first essential in an educated man is to speak well his mother tongue and be able to express his thoughts clearly and succinctly. It might also be added that in a sense the ability to speak and write well is the professional man's greatest commercial asset; for it is the one thing above all things that inspires respect and confidence of one's patrons and patients. In other words, a course in English might easily be considered a course in commercial pharmacy. The tragedy of the situation is and we must admit it, that a year in English does not do what we would like to have it do in correcting deficiencies in one's language. A number of teachers of English in schools of pharmacy have realized that English must be taught in a college of pharmacy beyond the courses in English routinely offered. Mrs. Adelaide Harris of the School of Pharmacy of Western Reserve University presents a paper in THIS JOURNAL which is brimming full of ideas as to the possibilities and methods of rectifying this deplorable English situation in our schools. Please note that the title of the paper is not English for Students of Pharmacy, but English for Pharmacists, and the paper can be read to advantage by every retail druggist in the United States.—RUFUS A. LYMAN, *Editor.*

ENGLISH FOR PHARMACISTS.

THE TEACHING OF ENGLISH IN SCHOOLS OF PHARMACY.

BY ADELAIDE E. HARRIS.*

On the door leading to the class rooms of the School of Pharmacy of Western Reserve University are two gold-lettered words, one beneath the other: Pharmacognosy. English. The words indicate the two departments located here, yet to the casual passerby, pausing to comment, they suggest a special kind of English, whose peculiar habitat is a School of Pharmacy.

Is there such a subject as Pharmacy English? One trusts not. The language spoken and written by the graduates of our schools does not, or at least should not, differ from the language used by other educated men. The books they read, in the moments torn from the perusal of the PHARMACOPŒIA and the NATIONAL FORMULARY, are those read by their peers. Our chief responsibility, then, as teachers of English, would seem to be to give our students so firm a foundation in the principles of speech and writing, as well as in the appreciation of good reading, that in both their professional and social relationships they would rank as cultivated men. "What, you mean that pharmacists have to take English? Well, they certainly need it." This is a comment heard less frequently of late, but one which should not be called for at all.

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There is no such subject as Pharmacy English; yet the fact remains that English in a school of pharmacy should be—obvious as it may sound—primarily for pharmacists. It should consider their particular needs, although these needs may not as yet be expressed or realized. The students in our classes to-day are enrolled for a four-year course, with the degree of Bachelor of Science as their goal. They wish to be considered professional men, whether their work is to lie in the retail store, the hospital pharmacy or the research laboratory. They will have an increasing leisure in which to develop their individual lives. The men and women in the other health professions, doctors, dentists, nurses, with whom they will be associated will have had from two to four years of work in a college of liberal arts before their four years of professional training, and they must not feel at too great a disadvantage with them. For these students a course should be planned that will not, on the one hand, be so narrow that it considers only their professional requirements, nor, on the other, be so vaguely cultural that it fails to have any connection with them.

Certain obstacles face us at the outset. The average freshman who enrolls in a school of pharmacy is not primarily interested in English. He may even be definitely antagonistic. He is, presumably, a science major, and though he may not shine in chemistry he recognizes its relevancy to his chosen career. What, indeed, has English to do with the filling of prescriptions? One freshman may be permitted to speak for the many: "Of all the subjects that engrossed me in high school I cannot truthfully say that English was my grand passion." And another, whose interests are clearly not cultural, utters this lament: "English, mathematics and botany, all comprehensive subjects, thoroughly discourage one and leave him in an uncertain state."

The question of whether the English courses should be taught within the school of pharmacy itself or in the university is one which cannot be ignored in this paper, although it cannot be answered. Probably in most of our schools there is no possibility of choice, and, even when there is, the varying circumstances would have to be taken into consideration. Inevitably, there must be advantages and disadvantages to either arrangement. At Western Reserve University conditions have dictated the teaching of English within the School of Pharmacy, although our students take their chemistry, mathematics and foreign languages in University classes. The benefits derived from such a plan can be suggested only by setting down in broad outlines the work of the Pharmacy English department at Western Reserve University. My hesitancy in doing so is due to the fear that to the slightest extent the courses so outlined should be assumed to be models. The main purpose of this paper is to provoke discussion. If it should bring suggestions or objections from others concerned with the teaching of English to pharmacy students, something might come of it which would be of definite value to us all.

As far as objectives go, the courses in English at Western Reserve are planned to meet the broad needs of the students. In this school, even in the days when a pharmacy degree could be gained in two years and pharmacy was that much nearer a business than a profession, the work in English was never considered "Business English." For as long as the School has been a part of the University, the English department has been the chief agent of culture, of "sweetness and light," in an atmosphere necessarily impregnated with chemical experiments, with the identifica-

tion of crude drugs, with the manufacture of tablets and ointments. It has assumed the responsibility of training for living as well as for making a living, of preparing for that increased leisure which must come—even for pharmacists.

English is a catholic course wherever it is found—in a professional school it must be particularly so. Without neglecting the practical side—and that side is to be developed later—no other course can so naturally take the lead in questions of good manners and good taste and of taking advantage of the cultural opportunities of the university and city.

Suggestions in these matters cannot be covered and dismissed at any one time, but are introduced throughout the year. Occasions are naturally provided. After the luncheon to welcome the freshmen and before the Parke-Davis or Eli Lilly trips, at the time of the girls' tea and the student council dance, interest is already aroused concerning table manners, introductions, the responsibility of contributing one's share to the conversation and like matters. Letter writing, particularly social notes and the letter of application, brings up other points of social usage. At Western Reserve the pharmacy freshmen go each year to the Cleveland Museum of Art, and the junior class visits a special exhibit. A few students are induced to attend the Playhouse or a special lecture through the privilege of substituting their reports for a regular theme; special problems send them all to the University library. In this phase of the English work, as in others, still more might be accomplished through the further support of the faculty. When our dean comments on an opera or play he has attended, when a popular professor of chemistry expresses shocked surprise that some members of his class have never been inside the Art Museum, the recommendations of a feminine English teacher are strongly enforced.

Within the last three years certain inexpensive pamphlets have simplified and strengthened the somewhat extraneous sides of the work. *The Technique of Good Manners* has been used as a reference for questions relating to etiquette and personal appearance, and other handbooks are recommended. *The Students' Guide of Efficient Study* is another required, though unrelated pamphlet, which is useful at the beginning of the year, since it treats such practical matters as planning work, note taking and learning to concentrate.

Granted that any social and cultural contributions that can be made by the English courses are of particular value in a professional school, they must not be developed at the expense of the practical side. Our students must be trained to speak and write clearly, accurately and with reasonable effectiveness; they must be trained to read with understanding and, wherever possible, with appreciation. Indeed a disproportionate amount of time must be spent upon the mechanics of English. The foundation which should have been laid in grammar and high school is possessed by only the exceptional college freshman, and often his family background and his environment are a handicap rather than an aid. The problem is not, it may be said, peculiar to a school of pharmacy, but it exists here and has to be faced.

Courses in Freshman English must resemble each other so closely that no one needs to be described in detail. The broad outlines alone will be indicated, and the emphasis placed upon those features which are particularly pertinent to our needs. The principles of composition are taken care of by the text which is used throughout the year. The perforated sheets of this text provide a thorough drill on

fundamentals and conserve the students' time. When these are corrected and the analysis of the results brought before the class, an attempt is made to stress only the more serious errors and to avoid the niceties of the purist. The mechanical elements—punctuation and grammatical construction, for example—are not considered as ends in themselves, but as aids to good sentences and hence to a more mature and flexible style. The need of clear thinking as a basis for clear writing must have been deeply impressed on the mind of one unhappy freshman to account for the following: "I also find English one of the hardest subjects I carry. It makes one think different from what I do on other subjects. This subject English is a real battle. As I have mentioned above you have to think and think clearly."

Theme writing is naturally the backbone of the first-year course. One or two short themes a week are required the first semester, with longer themes the second semester, each theme being corrected or rewritten and checked in conference. (The conference periods vary in length and frequency with the individual students, but they are held for all.) The type assigned is chiefly expository, a type which calls for definite structure; but for material, the writer is encouraged to draw upon his own interests and hobbies, experience and background. A limited time is devoted to letter writing, business and social, with the point always made that for the technical forms of business correspondence—sales letters, complaint letters and others—a recent text on the business letter should be consulted. Place is found for drill in vocabulary building and the intelligent use of the dictionary. Too little place can be found for oral talks, yet they are given whenever possible, particularly on outside reading.

Two written projects of the first year—the term paper and the library problem—have been adapted as far as possible to the interests of our students. The term paper provides an introduction to the technique of research, scientific or literary. It involves, in addition to careful organization, insured partly by the sentence outline, practice in the finding and handling of source material, the taking of notes on cards, the arrangement of foot-notes and the preparation of a bibliography. The subject matter may be drawn from the field of pharmacy but not necessarily so—there is still plenty of time for that. The appeal to the student is often made through giving him the opportunity to investigate a subject in which he is already interested, a hobby he has already made his own. It may be the breeding of tropical fish or the developments—in color photography, the building of model airplanes or the cultural achievements of his race—whatever the subject, this experience in the organizing and writing of a simple research paper should stand him in good stead in future courses and in personal investigation. It may also lay the foundation for an enduring interest which will bring its own reward.

The library problem is assigned at the beginning of the second semester some weeks before the term paper to which it is allied. Primarily, the project is designed to introduce the student to the tools of scholarship in any field, though particularly in his own, so that he may know the feel of them when he is called upon for simple research papers or reports. It helps also to impress upon him that the fact of being perfectly at home in a laboratory is no reason for feeling ill at ease in a library. Many of the questions are adapted to his professional interests. Let me illustrate by a few examples. The mechanics of the card catalog are revealed through the preparation of a bibliography of histories of pharmacy, and through the listing of

bibliographical data on such books as *Microbe Hunters* and *Rats, Lice and History*. In the *Encyclopedia Brittanica* the article, "Alchemy," may be looked up and the author and bibliography noted; in the *Encyclopedia of the Social Sciences* the article "Medical Materials Industry," is investigated and the cross-references listed. Almanacs and Year Books yield information not only on the increase in automobile fatalities and the outstanding motion pictures of the preceding year, but on important achievements in medicine and chemistry, the recent trends in drugs, the locations of schools of pharmacy. The *Book Review Digest* may be consulted for critical opinion on such books as *Devils, Drugs and Doctors* or *An American Doctor's Odyssey;* readers' handbooks and anthologies of quotations for allusions that disclose pharmacy in literature; the *New English Dictionary* for the earliest uses of the familiar terms: apothecary, druggist, pharmacist. The *Reader's Guide* and the *Industrial Arts' Index* are used to prepare a working bibliography for possible papers entitled; Recent Food and Drug Legislation or Federal Regulation of Narcotics.

At Western Reserve the emphasis is placed upon the principles and practice of composition the first semester and upon the understanding of literature the second, but there is no marked division in the work of the year. Neither has it been found practicable to make the easy distinction between writing as a tool for practical and professional purposes and reading as a source of personal enrichment. Accurate and forceful writing has surely a social and cultural value and the understanding of the written word a practical. A recent text on Business English stresses the importance of imagination in business and urges its cultivation through the reading of the best prose and poetry. There is a point here, though it may be open to question if literature read for that ulterior end would yield very much to the reader.

The anthology now used throughout the year in our first-year classes contains examples of biographical sketches, essays and articles, plays, short stories and poems, none earlier than the nineteenth century, the greater number of our own day. It supplanted another of the same type, largely on the grounds that *Florence Nightingale* would appeal to our students more than *Queen Victoria*. Likewise for *The Return of the Native* we have substituted *Arrowsmith*, in the belief that the picture of a young scientist driven by enthusiasm and curiosity to seek out the facts was of more significance for students of science than the tragic, fate-woven happenings on Egdon Heath.

The advisability of giving a survey course in the second semester should, it would seem, be gravely challenged, at least in a professional school. There was a time—it is best forgotten—when we undertook to follow the story of English literature from Caedmon to Kipling, with results that were too often profoundly discouraging. The fuddled state of mind of the sufferer who wrote in his final paper: "The language of Beowulf is French, it was written during the Age of Chaucer to the ascension of Queen Elizabeth," may have been extreme yet it is also revealing. Nor is the mere ability to identify great names an end in itself. Its value for social purposes has been argued, as did the student who wrote that "very seldom does one attend a ball or a yachting party without some mention of the immortal works of Shakespeare, Milton, Chaucer, or some of the other famous poets of the day being brought up," but the contingency here raised is, for most future pharmacists, too remote to demand consideration.

More important is training in the ability to understand what is read, to grasp the point of view of the writer though it is remote from one's own, to analyze, condense or restate in words that contain the spirit and intention of the original. To inculcate a love of reading, to kindle a desire to grasp the underlying thought of the author, to foster the idea that appreciation of literature, as of all the arts, is a matter of growth and continued contact—these are high aims, but we can probably come closer to attaining them if we devote the few hours we have to the writings that are close in time and in spirit to the students who read them. The use of the contemporary writing, requiring as it does a minimum of biographical and historical background, makes it possible to concentrate upon the form and content of the work itself, and thus to come closer to some measure of appreciation.

"Outside reading" is encouraged in various ways. The pamphlet, *Good Reading*, published by the National Council of Teachers of English, eliminates the need of preparing book lists, although to it must now be added the books published since 1935 that can be recommended. Indeed, the natural appeal of a number of recent books is on our side. The cry of "No time," justified to a certain extent by the long laboratory periods and necessary job, is a disheartening barrier; yet more needs to be done if that most rewarding of all habits, the habit of reading good books, is to be formed.

When the course in pharmacy was completed in two or three years, one year of English was all that could be included, regardless of the need. With the establishment of the four-year course leading to the B.S. degree and the consequent broadening and strengthening of the curriculum, the question of a second year of English can be seriously considered. A number of our schools have already done so. In at least six, two years are required, and in many more a second year is elective. Considering the natural trend, the second year, required or recommended, is to be increasingly expected.

Of what should that second year consist? The objectives of the first, candor would compel us to admit, are far from attained. Particularly does this apply to errors in grammar and diction. The defense is that crudities so deeply embedded that they have resisted the continuous war waged upon them through grammar and high school and have entered college cannot always be eradicated in one year. They may not be disposed of in two, although we trust the amount of time devoted to the process has a direct bearing upon the result. Yet if the desires of the students themselves are to be consulted we shall not offer a second course in composition. not at least under that name. The mingled feeling of resentment and dismay a number will cherish over being expected to take a second year of English (there was a time when one year was considered an effrontery) will not be placated by the prospects of another year of theme writing. At the same time they may respond to a course that seems to them to have a definite connection with their future work as pharmacists.

From incomplete data compiled from a number of catalogs, it would appear that our schools have given different answers to the problem. A course in public speaking is the first choice of a number, with courses in expository writing and English literature following. A careful investigation of this question would be helpful.

At Western Reserve the experimental period of the second year of English

may not have passed. For two years a combined course in public speaking and magazine article writing was required of all juniors; last year a one-year course, entitled Professional Speech, was made an elective but given a definite place in the curriculum. The writing course is now an elective of one semester, as are courses in the contemporary biography and the contemporary novel. There is no real expectation at present of encouraging students to take more than two years of English, although exceptions might be made.

The fact that the speech course this year was elected by the stronger students in the class leads to another important question. Might it not be wise deliberately to plan a course for these students we hope may be leaders in the profession, the men who in a few years may be on the faculties of our schools, editing and contributing to our journals, addressing and holding office in our associations and academies? Too few graduates of the two-year course are fitted for these positions, though such a statement must always be qualified by the admission that the amount of education is by no means the only factor in a man's success.

For the weaker students, those who make the English grade with difficulty but fulfil the science requirements sufficiently for graduation, some further experience with the fundamentals of composition should be arranged. One plan might be to require those students who do not elect the second-year course to take an examination in the mechanics of English, and, if they do not pass it, to take a brief, comprehensive review. It may well be that in those universities in which a sub-freshman or remedial course is required of all who do not pass the entrance examination in English, this procedure would be unnecessary.

The speech course at the School of Pharmacy of Western Reserve University is, to quote the catalog, planned with particular attention to the needs of the professional student. As a whole, the upper classmen welcome a course of this type, situations already encountered in the business and social world having convinced them of its importance. They feel, too, that the man who can speak clearly and persuasively, either informally in conference and committee or more formally on the platform, is a man to be respected. Gradually they discover that training in speech is training in other factors—organization, accuracy, logical thinking—no less needed but perhaps not so eagerly sought after.

The course as a whole is too orthodox in its methods to require presentation in detail. It emphasizes, as must every speech course, the ability to think on one's feet and to recreate one's thoughts with sincerity and conviction. It provides practice in the different types of speeches—the extempore, the impromptu and the written, with the emphasis upon the first-named. It provides training in the handling of group discussions, including the asking and answering of questions, in presiding over meetings and introducing speakers. It hopes also to produce discriminating audiences as well as performers.

With the effective delivery of the speech itself held as the goal, it is possible to weave into its preparation, drill in those essentials of composition—oral and written—that still need to be mastered. Definite organization is assured, or reasonably so, by the sentence outline or analysis which must be submitted in advance of the speech. New stimulus is provided for the exercises in vocabulary building, in pronunciation, even in the ruefully admitted errors of grammar and diction. Point is given to the finding and use of reference materials and to the employment

of the other tools of research. Particularly satisfying is the increased zeal for good reading evinced in reports that are often stimulating as well as intelligent.

All this could be added to and expanded, but the main point of the course is still to be made. That lies, it seems to me, in the close relationship it has with the other departments in the School. Its title, Professional Speech, itself implies that relationship. It is carried out as far as possible in the form and content of the speeches assigned, though not without the realization that the word "professional" is broad in its connotations and that the professional man should not be inarticulate on any subject but his own.

Illustrations are needed. The broader interests of the pharmacist as an individual are expressed in informative talks on current events, civic and national problems, interesting people and books; in entertaining talks which at least win the approval of the audience; in talks to stimulate or convince on anything from the need of a new ping pong table in the lounge to the need of a new interpretation of religion. One series, in the form of a symposium, drew the composite picture of an ideal student of pharmacy, each speaker contributing one point. This model student would be interested in the history of pharmacy, investigate the opportunities in his profession, keep abreast of the latest developments in medicine and pharmacy and—at the same time—take part in the activities of the School and University, take advantage of the cultural opportunities of Cleveland, keep informed of the news of the world, broaden his interests through general reading, cultivate a hobby and so on through a formidable, if not an alarming, list of virtues.

The main talks of the year, those given at the end of each semester, were on subjects almost exclusively related to pharmacy. The first series, made up of the talk to actuate was given during a long session, broken by recess and refreshments, and dignified by an augmented audience and especially appointed chairmen, ushers and critics. The final series was composed of written speeches read before the class, with the idea that since actual speeches prepared for formal or professional gatherings are so often read, practice in doing so as effectively as possible would not be amiss. The written speech is, moreover, a valuable exercise in expository writing—it actually takes the form of the research paper—but was made more palatable for the student by being prepared for a definite audience and occasion.

It is gratifying to record that some of the talks have had immediate and tangible results. To one is due the reorganization this year of a student branch of the American Pharmaceutical Association. This branch during the University Open House sponsored a speech contest on the general theme of the Value of Pharmacy. From the president of the Northern Ohio Druggists' Association has come the proposal that a student speech contest be held for its members. Perhaps, in this connection, it can also be stated that two student publications—the *Pharmacon* and *Mortar and Pestle*—provided needed outlets for papers and written speeches of special merit.

The correlation between the English courses, in particular the speech course, and other departments of the School of Pharmacy has been close, as this paper has attempted to point out. It could be even closer, with definite advantages for both. The dean and the other members of the faculty have coöperated in supplying topics for talks and papers, in responding to requests for interviews, in swelling the audience for special programs, in acting as judges in contests. They, in turn,

should expect for their own classes a higher standard in oral and written reports, a greater measure of originality, a more interesting presentation.

PINEAPPLE SYRUP.

BY BERNARD FANTUS AND H. A. DYNIEWICZ.*

The success, we believe, the Syrup of Cherry has achieved as a flavoring vehicle for acid medication, as evidenced by its acceptance in the National Formulary (VI), emboldened us to propose to ourselves the question whether it might not be well to make available to the physician for the flavoring of medicines some other fruit flavors such as apricot, peach or pineapple.

We have prepared Syrup of Peach, Syrup of Apricot and Syrup of Pineapple, following a general formula, such as is official in the National Formulary for Syrup of Cherry and Syrup of Raspberry. We find that of these the Pineapple Syrup is the only one that seems to have special virtues which might make it suitable as a vehicle for medicines. The Peach and Apricot flavors are somewhat too delicate to have much disguising value. Would, therefore, like to submit the following formula for consideration and possible inclusion in a subsequent edition of the National Formulary.

SYRUPUS BROMELIÆ

Syrup of Pineapple

Syr. Bromel.

Crush pineapple in a grinder, dissolve 0.1 per cent of benzoic acid in the mixture, and allow to stand at room temperature until a small portion of the filtered juice produces a clear solution when mixed with one-half of its volume of alcohol. Press out the juice from the mixture and filter; add sucrose in the proportion of 850 Gm. of sucrose to each 450 cc. of the filtered juice. Dissolve the sucrose in the juice by heat on a water-bath, cool and remove the scum. Add 20 cc. of alcohol for each 1000 cc. of Syrup.

Canned Pineapple juice might be employed in the above formula, although the use of the fruit, as above described, is much more economical.

Storage.

Keep the Syrup in well-closed containers.

Alcohol content: from 1 to 2 per cent, by volume, of C_2H_5OH.

We believe that the Pineapple Syrup has a special value as a vehicle for sodium citrate or potassium citrate for which the colored fruit syrups like cherry or raspberry are not suitable as the citrate causes a change in color. We welcome the trial of the following prescription:

℞	Potassium citrate	15 Gm.
	Water	15 cc.
	Syrup of Pineapple, to make	60 cc.

Label: Teaspoonful in one-half glassful of water every two hours.

Having wasted much time in a fruitless endeavor to develop an artificial cherry bouquet, we have arrived at the conclusion that it is beyond our wisdom and power to imitate artificially

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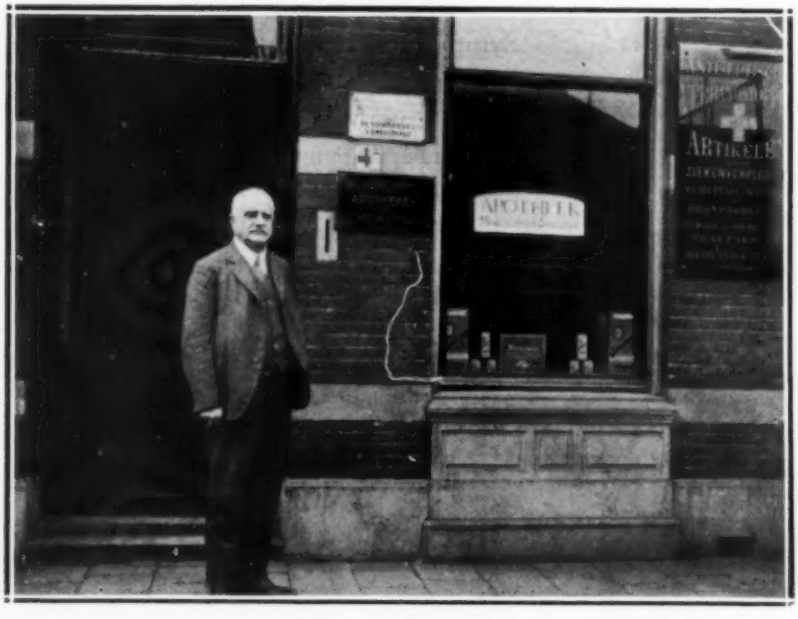
* From the Laboratory of Pharmacology and Therapeutics, University of Illinois, College of Medicine, assisted by a grant from the AMERICAN PHARMACEUTICAL ASSOCIATION.

that delicious bouquet that the inanimate plant is able to produce by an alchemy all its own. Especially to be avoided are such atrocious mixtures as the so-called "pineapple essences" with amyl and ethyl acetates and ethyl butyrate as their odoriferous ingredients. It is hoped that no pharmacist will be guilty of employing any of these "fruit essences" for the preparation of his soda fountain syrups, as the use of these differentiates the cheap soft drink parlor from the pharmacist's fountain where true fruit flavors are being dispensed. By the same token it should be considered an adulteration if any but the true fruit syrups are used in the compounding of prescriptions.

J. J. HOFMAN.

July 16th marked the completion of fifty years of service to pharmacy of our *Honorary Member*, Dr. J. J. Hofman. The event was celebrated with a jubilee meeting at the Departmental Headquarters in the Hague and a reception and dinner at the Hotel de Witte Brug. Dr. Hofman received the congratulations and felicitations of 160 guests and was also the recipient of many letters and telegrams from pharmacists and pharmaceutical associations both at home and abroad. He was awarded the gold medal of the Netherlands Pharmaceutical Association, an honor which in the past has been given only to Professor van der Wielen and to Professor Dr. L. van Itallie. Presiding at the jubilee was Professor van der Wielen, editor of the *Pharmaceutisches Weekblad*, whose remarks are published in the July 24th number of that journal and who is also the author of a sketch entitled "Dr. Jan Justus Hofman, Apotheker, 1887–1937," appearing in the July 10th number of the *Weekblad*.



DR. J. J. HOFMAN.

A sketch of Dr. Hofman also appears in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 20, 735 (1931). He was born June 1, 1866 in Alphen on the Rhine and at the age of 21 passed the examination for pharmacist having received his education in the public schools of the Hague and at the University of Leyden. After serving a year in a pharmacy at Utrecht he became pharmacist to the Hospital at Rotterdam and it was here that his activities began. His first published work concerns the quantitative determination of albumin in urine. He was a co-worker on the Supplement to the 3rd Netherlands Pharmacopœia published in 1891. Thus

began Dr. Hofman's scientific and association work and no year has since passed in which he did not publish one or more papers. Professor van der Wielen lists 123 alone, published in Netherland Journals, 119 in the *Pharmaceutisches Weekblad*.

In 1893 Dr. Hofman established a pharmacy in the Hague where he is still actively engaged in the practice of his profession and in the manufacture of fine pharmaceuticals. It was in the doorway of this pharmacy that Dr. Hofman stood when the writer of this sketch made the accompanying photograph in 1931.

Besides Dr. Hofman's scientific work and his many papers he has also held a number of distinctive positions, both civic and professional. For several years he was a member of the Council of the Netherlands Pharmaceutical Association serving as its president for fifteen years; he served on the Health Committee of the Hague and the Congress for Public Health Regulations and held many other positions on local and national committees in Holland.

Dr. Hofman was perhaps the prime-mover of the International Pharmaceutical Congress held at the Hague in 1913. It was at this meeting that he was elected secretary of the International Pharmaceutical Federation, a position he occupied until his election to its presidency at the Stockholm meeting in 1930. He was promoted to the doctorate at Leiden in 1929, the title of his dissertation being "Bijdrage tot de kennis der Indische Grasolies."

Professor van der Wielen says of him, "—the brilliant fulfillment of his career, his many publications and his devotion to pharmacy and to the Netherlands Pharmaceutical Association should cause all Dutch pharmacists to look back over these fifty years with gratitude; Hofman's retrospective view of his own versatile accomplishments must be one of great satisfaction."—E. H. WIRTH.

CENTENARY OF THE DEATH OF CHARLES FREDERICK CHANDLER.

National Science organizations will join with Columbia University in a series of events from October 6th to November 4th in commemorating the one hundredth anniversary of the death of Charles Frederick Chandler, father of modern industrial chemistry and the first Public Health scientist of New York City. He was a founder of Columbia School of Medicine in 1864 and of the American Chemical Society in 1876. He was born on December 6, 1836 and died on August 25, 1925. He became a member of the A. PH. A. in 1867—a sketch may be found in the March number for 1917, on page 227, and also in the September number, 1925, page 849.

Pharmacy willingly and gladly joins the scientific organizations in honoring the memory of one who highly regarded pharmacy as a profession.

The program embraces three Chandler memorial lectures in the fields of chemistry, medicine and public health. The presentation of the Chandler medal of Columbia University to Dr. John Howard Northrup, of the Rockefeller Institute for medical research, and a Chandler Centennial Dinner at the Waldorf-Astoria, are parts of the program.

The second lecture on October 13th will be given by Dean William de MacNider of the University of North Carolina School of Medicine, who will speak on "Certain Recent Developments in Chemistry and Their Bearing on Cellular Activity."

Dr. Wm. J. Schieffelin of New York, a former student of Professor Chandler and Honorary President of the School of Pharmacy of Columbia University, will be Chairman. Dr. Haven Emerson, Director of the Institute of Public Health in the School of Medicine, will be the third lecturer, speaking on October 20th on "New York's First Public Health Chemist." Prof. Daniel D. Jackson, Head of the Department of Chemical Engineering, will preside. The Centennial dinner will take place at the Waldorf-Astoria, on November 4th. The speakers will be Dr. Nicholas Murray Butler; Dr. Willis Rodney Whitney, the 1920 medalist; and Dean Frank Clifford Whitmore of the College of Physics and Chemistry, and President-Elect of the American Chemical Society.

Liberty is taken for abstracting the larger part of this item from *Science* of September 24th.

EDITORIAL NOTES

EXAMINATION OF PHARMACISTS FOR THE MEDICAL ADMINISTRATIVE CORPS, REGULAR ARMY.

The War Department is announcing an examination December 13–17, 1937, to qualify candidates for appointment as Second Lieutenant in the Medical Administrative Corps, Regular Army, to fill the ten existing vacancies.

Appointments will be made from pharmacists, male citizens of the United States, between the ages of 21 and 32 years, who are graduates of recognized schools or colleges of pharmacy, that is, schools or colleges approved by the American Association Colleges of Pharmacy, requiring four years of instruction for graduation and legally authorized to confer the degree of Bachelor of Science in Pharmacy.

Examination for appointment includes physical, a written examination in Practice of Pharmacy, Pharmaceutical Chemistry, Pharmacognosy, Pharmacology, and Bacteriology, Hygiene and Sanitation, and an estimate of the candidate's adaptability for military service.

Examining boards will be convened at convenient locations throughout the continental limits of the United States for the examination of candidates authorized by the War Department to appear before them. Full information and application blanks will be furnished upon request by The Adjutant General, War Department, Washington, D. C.

Applications will not be considered after November 24, 1937.

PROGRAM, AUTUMN 1937 MEETINGS OF THE WASHINGTON BRANCH, AMERICAN PHARMACEUTICAL ASSOCIATION.

OCTOBER 18, 1937.

(1) Survey of the Bioassays of the U. S. P. XI and N. F. VI.....William T. McClosky.

(2) Color Names for Pharmaceuticals (Illustrated with Charts)...K. L. Kelly.

(3) Reminiscences of Veteran Pharmacists and Pharmaceutical Chemists of Washington.

(FIVE-MINUTE SKETCHES.)

Henry E. Kalusowski.....S. L. Hilton.
M. I. Wilbert.....S. L. Hilton.
H. W. Wiley.....L. F. Kebler.

NOVEMBER 15, 1937.

Some Native Poisonous Plants.
(Illustrated).....James F. Couch.
Discussed by V. K. Chesnut.

DECEMBER 13, 1937.

Pharmacy and Medicine in Ancient Egypt.
(Illustrated).....L. E. Warren.
A popular lecture, Ladies particularly invited.
A Dinner Meeting is in prospect. Date to be announced.

Announcement has recently been made that the work of preparing the new edition of the French Codex has now been completed and that the new Pharmacopée Française is to appear during the course of this year. The new edition, which takes the place of the 1908 edition, reprinted with additions in 1920, and further added to since by various additions, will be in two volumes, the first containing the legal section with general chemical information, and the second including a list of chemical, medical and veterinary products. This new Codex has been compiled by a commission which included professors of the Paris School of Medicine and Pharmacy, as well as representatives from the various retail chemists' organizations. The secretary-general of the commission is Charles Lormand, director of the Control Laboratory for Medicines.

PHARMACY WEEK.

Pharmacy Week this year is held from October 18th to 23rd. The success of the movement depends upon the activities of the pharmacists. The greater the number who take part the greater will be the results. All are urged to take part.

Publicity for Pharmacy Week is best prepared by individual effort according to locality: By displays, distribution of messages, mailing communications to allied professions, the press, conversations with patrons, talks before clubs and other civic organizations, high school essays, etc. Publicity should be on professional lines.

Keep in mind the prizes that are offered, the certificates for meritorious displays; the Robert J. Ruth Memorial Prize becomes the permanent possession of the winner.

NEW AND NONOFFICIAL REMEDIES.

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.—PAUL NICHOLAS LEECH, *Secretary*.

MERCURIN.—A mixture of 20 per cent of the β-methoxy-γ-hydroxymercuri-propylamide of trimethyl cyclopentane dicarboxylic acid $C(CH_3)_2C.CH_3.COOH.CH_2CH_2CHCONHCH_2CH_2.OCH_3.CH_2HgOH$ and 80 per cent of its sodium salt. Mercurin is a complex synthetic mercurial containing about 40 per cent of mercury prepared from *d*-camphoric acid and a racemic substituted propylamide.

Actions and Uses.—Mercurin is proposed for use as a diuretic to be administered rectally. Its potency is comparable to that of parenterally administrated mercurial diuretics. It is well tolerated. It is contraindicated in advanced chronic nephritis and acute renal disease and should be used with caution in presence of diarrhea, enterocolitis and hemorrhoids or other rectal disorders. It probably acts as a mild renal irritant.

Dosage.—Mercurin is supplied in the form of cocoa butter suppositories, each containing 0.5 Gm. of mercurin, to be administered rectally in the morning, repeated at three- to five-day intervals as required by each individual case.

Manufactured by Chinoin Chemical and Pharmaceutical Works, Ltd., Budapest, Hungary (Campbell Products, Inc., New York, distributor), U. S. patent applied for. U. S. trademark 338,989.

Mercurin Suppositories, 0.5 Gm.

Mercurin occurs as a white, odorless, bitter tasting noncrystalline powder that is very slightly soluble in water, soluble in alcohol, and insoluble in ether. An aqueous solution has a p_H of about 7.8. Suspend about 1 Gm. of mercurin in 10 cc. of water, add 30 cc. of 2 normal acetic acid and 1.5 Gm. of ammonium chloride; heat on the water-bath and bubble hydrogen sulfide through the solution until no more precipitate is formed, filter while hot and place the filtrate in the refrigerator for twelve hours; filter and wash the crystals with a little cold water and dry at 75° C.: the precipitate with hydrogen sulfide indicates the presence of mercury; the crystals melt at from 157.5° to 158.5° C. and are identified as trimethyl cyclopentane dicarboxylic acid monoallylamide. Transfer about 1 Gm. of mercurin, accurately weighed, to a 25-cc. standard flask, add 1 cc. of sodium hydroxide solution, fill to the mark with water; observe the rotation of the resulting solution within thirty minutes in a layer 200 mm. thick at 25° C. using the D line of sodium: $[\alpha]_D^{25}$ is not less than 9.5 nor more than 10.5.

Saturate with hydrogen sulfide, 5 cc. of the solution prepared for observing the rotation: no precipitate forms and no coloration results (*Heavy metals—especially mercuric ions*). Dissolve 0.1 Gm. in 5 cc. of water, add 1 cc. of diluted nitric acid, filter through paper and divide the filtrate into two portions; to one portion add 1 cc. of silver nitrate solution: not more than a slight opalescence results (*chlorides*); to the other portion add 1 cc. of barium nitrate solution: no turbidity results (*sulfates*). When tested for arsenic according to the U. S. Pharmacopœia X, the product meets the requirements for arsenic (p. 428, Arsenic Test).

Transfer about 0.5 Gm. of mercurin, accurately weighed, to a wide mouth weighing bottle and dry to constant weight in an oven at 80° C.: the loss in weight is not less than 6.5 per cent nor more than 7.5 per cent. Determine nitrogen by the micro Dumas method: the nitrogen is not less than 2.75 per cent nor more than 2.80 per cent when calculated to the dried substance. Transfer an accurately weighed specimen of the original to a platinum dish and ash in the presence of sulfuric acid, ignite to constant weight in a muffle furnace at 900° C.: the residue calculated as sodium sulfate is equivalent to not less than 4.20 per cent nor more than 4.70 per cent sodium when calculated to the dried substance. Transfer about 0.3 Gm. of mercurin, accurately weighed, to a large platinum dish, add 15 cc. of a solution of sodium sulfide (made by dissolving 50 Gm. of crystallized sodium sulfide to make 100 cc. of solution) and sufficient water to nearly fill the dish, electrolyze at 5 volts for eighteen hours; siphon off the solution while adding water until the ammeter shows that no current is flowing; break the circuit; wash the mercury deposit with alcohol and ether; dry for a few minutes in a warm place; and then in a desiccator over sulfuric acid in which a beaker containing mercury has been placed, weigh: the percentage of mercury is between 30.2 per cent and 40.2 per cent when calculated to the dry basis.

MERCURIN SUPPOSITORIES.

Place a suppository in a beaker containing 150 cc. of cold anhydrous ether. When disintegration is complete, transfer the undissolved material to a prepared gooch crucible using the first filtrate as needed to complete the transfer, dry the crucible in an oven at 80° C., cool in a desiccator and weigh: the weight of the insoluble material is not less than 0.47 Gm. or more than 0.53 Gm., and it meets the standards for mercurin.—From *J. A. M. A.*, July 10, 1937.

PERSONAL AND NEWS ITEMS.

It is regretted that the name of **Mrs. Robert S. Lehman** was omitted from the List of Registrants in the August JOURNAL. She was *Chairlady* of the Ladies' Committee at the New York Meeting.

Mr. and Mrs. Herbert Skinner, of England, were visitors at the AMERICAN INSTITUTE OF PHARMACY, Washington. Mr. Skinner is pharmacist at the Royal Northern Hospital, London; he is an *honorary member* of the AMERICAN PHARMACEUTICAL ASSOCIATION.

Former President, A. PH. A., **R. L. Swain** is president of the National Association of Boards of Pharmacy.

J. Leon Lascoff will be awarded the Remington Medal, for 1937, at a dinner in New York, on October 25th.

J. W. Gayle, *Secretary* of Kentucky Pharmaceutical Association, has been elected *Honorary President* of the National Association Boards of Pharmacy; he is also the *Treasurer*.

Secretary H. C. Christensen, N. A. B. P., and Mrs. Christensen were visitors at the AMERICAN INSTITUTE OF PHARMACY, on September 19th.

President E. N. Gathercoal, A. PH. A., and Mrs. Gathercoal, after a delightful visit through New England, stopped over at the AMERICAN INSTITUTE OF PHARMACY before returning to Chicago.

RODOLFO ALBINO DIAS DA SILVA.

We are advised by Virgilio Lucas, President of the Pharmaceutical Association of Brazil, of the death of Rodolfo Albino Dias da Silva, professor of Pharmacognosy at the School of Pharmacy, University of Brazil, late *honorary member* of the AMERICAN PHARMACEUTICAL ASSOCIATION. He has been succeeded by Professor Oswaldo de Almeida Costa, a pharmacologist of high standing. President Lucas advises that the latter has signified his interest in pharmacy and is a worthy successor.

OBITUARY.

DR. GEORGE H. SIMMONS.

A very large circle of friends among American physicians and pharmacists have been grieved to learn of the death of George H. Simmons, September 1st, at St. Luke's Hospital, Chicago, following an abdominal operation from which he failed to rally.

Courtesy J. A. M. A.
DR. GEORGE H. SIMMONS.

Dr. Simmons was born at Moreton, England, in 1852, and came to the United States when 18 years of age. While in attendance at the University of Nebraska he acted in an editorial capacity and as correspondent for various lay publications. He received the degree of M.D. from the Hahneman Medical College, Chicago, in 1882 and from the Rush Medical College in 1892.

He was engaged in the practice of medicine at Lincoln, Neb., from 1884 to 1892. In 1896 he established the *Western Medical Review*, of which he was the editor, and from 1895 to 1899 served as Secretary of the Nebraska State Medical Society.

In 1899 he became General Secretary of the American Medical Association and editor of *The Journal*, and at the time of his death was editor and general manager emeritus of that publication.

During the decade 1920–1930 he was a member of the Board of Trustees of the United States Pharmacopœial Convention. During the World War he held the rank of Major in the Army Medical Reserve Corps for which service he was awarded the distinguished Service Medal in 1921.

With the beginning of his service as General Secretary of the American Medical Association that rather staid professional organization entered upon a new order of existence. From a dignified professional society meeting periodically for the discussion of scientific papers it became an aggressively militant organization in the work of medical reform. Through its special organ it attacked medical quackery and fraud in all its forms. It led a crusade in favor of the improvement of the methods of medical education and in the exposure of fraudulent degree-conferring institutions.

Under his administration the A. M. A. Council on Pharmacy and Chemistry was established, through which the method of advertising therapeutic agents to the medical profession has been radically reformed, and at the same time the *Journal* has conducted a pitiless exposure of fraudulent medicines advertised to the general public.

It may fairly be said that it has been due mainly to his organizing and administrative ability that the American Medical Association has come to be regarded as the most potent and effective organization of its kind, and that the *A. M. A. Journal* owes its commanding

position among medical publications of the world.

It may fairly be said that through his work in the A. M. A. and its *Journal* Dr. Simmons has made a deeper and more lasting impression upon the practice of medicine than any other man of his generation.

In Lincoln, Neb., Dr. Simmons became known as a leader in reform movements and a resolution adopted by the Lincoln Chamber of Commerce indicated the willingness to admit the debt of that city to him for its political cleanliness and financial soundness.

The progress of the American Medical Association and its publications and other promotions have been brought into the sketch of Dr. Simmons, published in the *Journal A. M. A.* of September 4th. The article closes with the following lines: "The medical profession of the United States owes him a debt which it could never pay and which he never wished to collect."

We are indebted to Dr. James H. Beal for some of the foregoing data.

WILLIAM A. SAILER.

William A. Sailer, former director of Sharp & Dohme, and head of the Baltimore Drug Exchange, died September 19th, at Union Memorial Hospital, Baltimore, age 75 years. Mr. Sailer became director of Sharp & Dohme in 1908, holding the position until his retirement. He was born at Swedesboro in 1861 and received his early education at St. Louis. After the death of his father he returned to Swedesboro and entered the drug business and thereafter matriculated at Philadelphia College of Pharmacy and studied at the Medical and Chirugical College. Before going to Baltimore Mr. Sailer was associated with John Wyeth & Bro., Philadelphia.

He was three times president of the American Drug Manufacturers' Association; twice president of the Baltimore Drug Exchange. He was a member of the Union League of Philadelphia, the Military Order of the Loyal Legion, of Baltimore Country Club and the City Club.

He is survived by his widow and four children: Mrs. Philip M. Brown, Essex Fells, N. J.; Mrs. Paul E. Laferty, Baltimore; Miss Elizabeth G. Sailer of Baltimore; and John Wyeth Sailer of Philadelphia.

SOCIETIES AND COLLEGES.

N. A. R. D. MEETING.

The 1937 meeting of the N. A. R. D. convened in St. Louis, September 27th to October 1st, and promises to be very important and largely attended. The activities have extended from year to year and the responsibilities have increased greatly; this year they were of unusual importance and were given the consideration deserved, so that the foundations for practice under recent enactments may be properly adjusted, with fairness to all concerned. While this represented a very important part of the St. Louis program there was other legislation and conduct of business which made the coming together from near and far well worth the coming together for discussion and action for help and profit.

NEW HAMPSHIRE PHARMACEUTICAL ASSOCIATION.

The New Hampshire Pharmaceutical Association was held September 12th–14th, at "The Balsams," Dixville Notch, N. H., in the center of America's Switzerland, on beautiful Lake Gloriett. The convention was largely attended and speakers of prominence were in attendance; among them, President E. N. Gathercoal of the A. Ph. A., R. L. Swain, President of the N. A. B. P., and H. C. Christensen, Secretary of the N. A. B. P.

The address of President Moulton covered many important points, among these changes of several by-laws and a discussion of the New Hampshire plan, and phases of the activities of his term of office. President Moulton has completed a most successful year.

Among the speakers, besides those heretofore mentioned, were Dr. Howard E. Thompson of Nashua. He presented a motion picture of Alaska with descriptions of the country. Dr. Thompson is a well-known sportsman and surgeon and his address was well received.

A feature of the meeting was a presentation of badges to former presidents and officers who had given generously of their time to pharmaceutical affairs.

The annual banquet, followed by the President's ball, was a Monday night feature.

Under arrangement of President Moulton and the hospitalities of the members the visitors enjoyed a most interesting tour through the White Mountains.

The following officers were elected for the ensuing year:

President, George A. Moulton, Peterborough; *First Vice-President*, Charles E. Green, Pittsfield; *Second Vice-President*, George A. Clark, Nashua; *Secretary*, Arthur O. Burque, Nashua; *Treasurer*, A. E. Gosselin, Manchester; *Auditor*, Herbert E. Rice, Nashua.

MASSACHUSETTS AMENDMENTS.

Massachusetts amendments to the pharmacy laws which became effective August 24th.

For the first time in this state, it legalizes the activities of the Assistant Pharmacist during the temporary absence of the Registered Pharmacist, same not to exceed six (6) hours in any one day.

In case of enforced absence as a result of illness or accident, the Board of Pharmacy, upon proper application, may allow the Assistant the right to carry on the usual activities of a drug store during the enforced absence of the Registered Pharmacist.

The new law also confines the sale of hypnotics and all medicines prepared for hypodermic use in the human system to drug stores.

It gives the Board of Pharmacy for the first time the authority to make such rules and regulations as it deems necessary to properly enforce the provisions of law relating to the retail drug business, and to any other matter within its jurisdiction.

Chairman John F. Walsh of the Board of Pharmacy in a recent address made at the State Convention in Swampscott on June 2nd had this to say about the new Pharmacy Law. "We trust that with our new Pharmacy Bill behind us we will be able to make rules and regulations that will protect those who are in the profession at the present time." Chairman Walsh also solicited the advice of our Counsel, Mr. Silverman, in framing the new rules and regulations.

The enactment of this law, it is quite evident on the face of it, should be of more than passing significance to every drug store operator in Massachusetts.

At a meeting of the Board of Directors of the Massachusetts State Pharmaceutical Association held in Boston on August 23rd, Charles F. Brown of Fall River and Charles Kilmoski of Holyoke were elected directors to fill vacancies existing on the Board.—F. F. FINNERAN, through *the Apothecary*, September 1937.

Vermont Pharmaceutical Association held a one-day meeting in Rutland, September 20th, at the Meade Community House.

The *Connecticut Capsule*, filled by Alice-Esther Garvin, contains much news, quickly told. If the capsule is placed for investigation, the reader would interpret the capsule's message as "much in little."

A new monthly publication, the *F. S. P. A. Journal* (Florida), will make its initial appearance late in September. The new magazine will be distributed to every druggist in the state, regardless of membership in the State Association. President R. Q. Richards will be editor-in-chief.

The fall meeting of the Maryland Pharmaceutical Association will be held at Braddock Heights, Thursday, October 14th.

On account of the preparation for the November JOURNAL—"the Proceedings Number" of the ASSOCIATION—this issue of the JOURNAL is somewhat belated. It is hoped to restore and correct the Roster of Associations in a succeeding number and also list the Branches.

NEW OFFICERS FEDERAL WHOLESALE DRUGGISTS' ASSOCIATION.

In the annual election for officers the association selected the following: *President*, George A. Raab, Providence, R. I.; *Vice-President*, S. C. James, Buffalo, N. Y.; *Secretary*, R. E. Lee Williamson, Baltimore, Md.; *Treasurer*, O. J. Schmitz, Atchison, Kan.; *Sergeant-at-Arms*, Paul Pearson, Washington, D. C.

Experiments of H. H. Fricke and K. L. Kaufman with pure samples of these alkaloids lead to the conclusion that both are more stable in ether than in chloroform solutions. Continued heating on a water-bath causes their partial decomposition. The results show that heat is definitely a factor in the disappearance of atropine and hyoscyamine from ether solutions. When chloroform was used as the solvent, some other form of destruction must also have occurred, as the dried chloroform gave higher results than the U. S. P. grade.—Scientific Section, A. PH. A.

A method has been devised employing $PdCl_2$ for the detection of CO in O_2. Its applicability as an official procedure has been studied and presented in Scientific Section, A. PH. A., New York meeting, by F. K. Bell and John C. Krantz, Jr.

DR. CHARLES MOORE.

Upon attaining the ripe age of 82 years, Dr. Charles Moore has resigned the Chairmanship of the Commission of Fine Arts which he has held since 1915, and has been succeeded by Gilmore D. Clark who has been the vice-chairman for several years. Dr. Moore will continue as a member of the Commission to which he was named when it was established in 1902. Prior to that time he had served with the so-called McMillan Commission and has given his life to the development of the National Capital and of the fine arts in America—as was well said, this resignation "officially ends a career of great service to the country and particularly to the Capital City."

Dr. Moore took a great interest in the location and erection of the Headquarters Building and was a very helpful advisor and guide in this entire project. He spoke at the ground-breaking exercises in 1932 and at the dedication in 1934, and was at that time elected an Honorary member of the ASSOCIATION. He was a close friend of Sir Henry Wellcome with whom he served for many years on the board of the Gorgas Memorial.

In Dr. Moore, the ASSOCIATION and American Pharmacy has had a strong friend, who, it is hoped, will be spared for many more years of useful and unique service to his country.

THE PHARMACY EXHIBIT AT DALLAS AND CHICAGO.

The Pan-American Exposition at Dallas will be closed on October 31st and Dr. H. C. Christensen has gone to Dallas to arrange for the shipment of the Pharmacy Exhibit to Chicago for use later in the permanent Museum of Science and Industry in Jackson Park, which has been endowed by the late Julius Rosenwald. Over $3,000,000 is being spent in renovating and rearranging the interior of the Fine Arts Building of the 1893 Columbian Exposition, to house the Museum. The Pharmacy Exhibit will be permanently included among the Medical Science Exhibits, the cost of installation and maintenance to be borne by the Museum.

The Pharmacy Exhibit at Dallas was located in the Government Building with the other public health exhibits, during the seasons of 1936 and 1937. It has been inspected by many prominent persons and, with the exhibit at the Century of Progress Exhibition in Chicago, has brought Pharmacy and its services to the favorable attention of many thousands of visitors. Arrangements are already in progress for similar exhibits at the coming expositions in New York and San Francisco, and this seems now to have become a permanent activity of the A. PH. A.

The ASSOCIATION is indebted to Dr. Christensen who has directed each of these exhibits and to Miss Esther H. Barney who has been in daily charge of them. Miss Barney was also officer in charge, during the season of 1937, of all of the medical exhibits of Dallas, which were under the general supervision of the U. S. Public Health Service, and has served very acceptably in this important position. She has now been appointed to superintend the packing and shipping of these exhibits which is a further recognition of her ability in this field, and will be in Dallas until the close of the year.

Dr. Joseph Peter Hoguet, a surgeon of long and varied experience, has been appointed as Administrative Assistant and Medical Director of the New York World's Fair of 1939. In this position Dr. Hoguet will be in charge of the executive and administrative work of the Division of Public Health, Medicine and Sanitation. He will also be responsible for the health of members of the exposition staff and other employees and of visitors attending the Fair when the latter is opened to the public.

A. L. I. WINNE.